

10/501318

\*\*\*\*\* INVENTOR RESULTS \*\*\*\*\*

=> d his 155

(FILE 'HCAPLUS' ENTERED AT 09:05:21 ON 04 AUG 2007)

L55 13 S L54 AND L22

=> d que 155

L1 1 SEA FILE=HCAPLUS ABB=ON PLU=ON US20050148661/PN  
L22 QUE ABB=ON PLU=ON AY<2004 OR PY<2004 OR PRY<2004 OR MY  
<2004 OR REVIEW/DT  
L43 9 SEA FILE=HCAPLUS ABB=ON PLU=ON GAMELIN L?/AU  
L44 53 SEA FILE=HCAPLUS ABB=ON PLU=ON GAMELIN E?/AU  
L45 32 SEA FILE=HCAPLUS ABB=ON PLU=ON BOISDRON CELLE M?/AU  
L46 499 SEA FILE=HCAPLUS ABB=ON PLU=ON MOREL A?/AU  
L47 551 SEA FILE=HCAPLUS ABB=ON PLU=ON L43 OR (L44 OR L45 OR L46)  
L48 53 SEA FILE=HCAPLUS ABB=ON PLU=ON L44 AND (L45 OR L46 OR L47)  
L49 32 SEA FILE=HCAPLUS ABB=ON PLU=ON L45 AND (L46 OR L47)  
L50 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L43 AND L44 AND L45 AND L46  
L51 23 SEA FILE=HCAPLUS ABB=ON PLU=ON L47 AND L48 AND L49  
L52 23 SEA FILE=HCAPLUS ABB=ON PLU=ON L50 OR L51  
L54 22 SEA FILE=HCAPLUS ABB=ON PLU=ON L52 NOT L1  
L55 13 SEA FILE=HCAPLUS ABB=ON PLU=ON L54 AND L22

=> d his 172

(FILE 'MEDLINE, BIOSIS, EMBASE, BIOTECHNO, DRUGU' ENTERED AT 09:14:57 ON  
04 AUG 2007)

L72 14 S L50 NOT L70

=> d que 172

L10 QUE ABB=ON PLU=ON OXALATE OR OXALIC ACID  
L11 QUE ABB=ON PLU=ON OXALIPLATIN  
L13 QUE ABB=ON PLU=ON MAGNESIUM (2A) (SULFATE OR PIDOLATE)  
L14 QUE ABB=ON PLU=ON CANCER? OR NEOPLAS? OR TUMOR? OR TUM  
OUR?  
L15 QUE ABB=ON PLU=ON ANTIVIRAL? OR ANTI(W)VIRAL? OR VIRUS  
? OR ANTIVIRUS? OR ANTI(W)VIRUS?  
L16 QUE ABB=ON PLU=ON ?VIRUS? OR ?VIRAL?  
L17 QUE ABB=ON PLU=ON NEUROTOXIC?  
L22 QUE ABB=ON PLU=ON AY<2004 OR PY<2004 OR PRY<2004 OR MY  
<2004 OR REVIEW/DT  
L24 56622 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 OR L11  
L27 110313 SEA FILE=HCAPLUS ABB=ON PLU=ON CALCIUM/OBI (2A) (GLUCONATE/OB  
I OR CHLORIDE/OBI OR BROMOGALACTOGLUCONATE/OBI OR CARBONATE/OBI  
)  
L28 19480 SEA FILE=HCAPLUS ABB=ON PLU=ON MAGNESIUM/OBI (2A) (SULFATE/OB  
I OR PIDOLATE/OBI)  
L39 1286494 SEA FILE=HCAPLUS ABB=ON PLU=ON (TREAT#/OBI OR TREATMENT#/OBI  
OR PREVENT#/OBI OR CURE#/OBI)  
L41 254740 SEA FILE=HCAPLUS ABB=ON PLU=ON INJECT#/OBI OR ORAL#/OBI  
L43 9 SEA FILE=HCAPLUS ABB=ON PLU=ON GAMELIN L?/AU  
L44 53 SEA FILE=HCAPLUS ABB=ON PLU=ON GAMELIN E?/AU  
L45 32 SEA FILE=HCAPLUS ABB=ON PLU=ON BOISDRON CELLE M?/AU  
L46 499 SEA FILE=HCAPLUS ABB=ON PLU=ON MOREL A?/AU  
L50 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L43 AND L44 AND L45 AND L46  
L56 52321 SEA L24  
L57 61889 SEA L27  
L58 18226 SEA L28

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L59 78565 SEA L57 OR L58  
L60 947 SEA L56 AND L59  
L61 53 SEA L60 AND L14  
L62 5 SEA L60 AND L15  
L63 10 SEA L60 AND L16  
L64 25 SEA L60 AND L17  
L65 63 SEA (L61 OR L62 OR L63 OR L64)  
L66 42 SEA L39 AND L65  
L67 25 SEA L41 AND L65  
L68 47 SEA L66 OR L67  
L69 17 SEA L68 NOT L13  
L70 9 SEA L69 AND L22  
L72 14 SEA L50 NOT L70

=> dup rem l55 l72

FILE 'HCAPLUS' ENTERED AT 09:24:54 ON 04 AUG 2007  
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PROCESSING COMPLETED FOR L55  
PROCESSING COMPLETED FOR L72  
L74 19 DUP REM L55 L72 (8 DUPLICATES REMOVED)  
ANSWERS '1-13' FROM FILE HCAPLUS  
ANSWERS '14-15' FROM FILE MEDLINE  
ANSWERS '16-17' FROM FILE BIOSIS  
ANSWER '18' FROM FILE EMBASE  
ANSWER '19' FROM FILE DRUGU

=> d 1-13 ibib ab

L74 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2  
ACCESSION NUMBER: 2006:480609 HCAPLUS Full-text  
DOCUMENT NUMBER: 145:201737  
TITLE: Oxaliplatin neurotoxicity  
AUTHOR(S): Gamelin, Laurence; Boisdron-Celle,  
Michele; Morel, Alain; Gamelin,  
Erick  
CORPORATE SOURCE: Service de toxicologie, Centre Antipoisons, CHU  
Angers, Fr.  
SOURCE: Bulletin du Cancer (2006), 93(Spec.), S17-S22  
CODEN: BUCABS; ISSN: 0007-4551  
PUBLISHER: John Libbey Eurotext  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: French

AB A review. Oxaliplatin is a reference drug in the treatment of digestive-tract tumors, especially colorectal cancer. Its toxicity profile is dominated by a peripheral sensitive neuropathy, with neuromuscular manifestations. This neurotoxicity has 2 components: an acute toxicity characterized by a rapid

onset of cold-induced distal dysesthesia and/or paresthesia, muscular contractions, numbness, stiffness, usually transient but able to evolve into a chronic, persistent sensory peripheral neuropathy that eventually causes functional impairment. A persistent sensory peripheral neuropathy may develop with prolonged treatment, eventually causing superficial and deep sensory loss, sensory ataxia and functional impairment. This neurotoxicity is frequent, 80 % of the patients and becomes chronic in 15 to 20 % of the patients, sometimes irreversible. The mechanism of this neurotoxicity has been elucidated: an increased neuronal excitability is due to the action of oxaliplatin on voltage-gated sodium channels through chelation of calcium by the oxaliplatin metabolite. The prevention of this neurotoxicity is a major goal, taking in account the wide indications of this drug. Different approaches have been or are evaluated, based on pathogenic or practical concepts: (1) modifications of the administration schedule; (2) substances acting upon sodium channels: calcium-magnesium, carbamazepine, gabapentine, venlafaxin; (3) detoxifying agents and antioxydants: glutathion, amifostine,  $\alpha$ lipoic acid, tocopherol; (4) substances used in other kinds of neuropathy: glutamine,  $\alpha$ lipoic acid; (5) neurotrophic factors: NGF, LIF; (6) oxaliplatin analogs, with a DACH platin, without oxalate. Calcium-magnesium infusion seem to be an efficient and safe approach. Further studies are necessary for a better understanding and prevention of this neurotoxicity, potentially severe.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:719204 HCAPLUS Full-text

DOCUMENT NUMBER: 139:240336

TITLE: Diagnosis of cancer chemoresistance by quantitative RT-PCR analysis using an internal control template derived from multiple chemoresistance-related genes

INVENTOR(S): Gamelin, Erick; Morel, Alain; Boisdron, Celle Michele; Barbado, Maud

PATENT ASSIGNEE(S): Universite d'Angers, Fr.; Centre Anti-Cancereux P Papin

SOURCE: Fr. Demande, 58 pp.

CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2836918	A1	20030912	FR 2002-2844	20020306 <--
PRIORITY APPLN. INFO.:			FR 2002-2844	20020306 <--

AB This invention relates to diagnosis of cancer chemoresistance in human biol. samples, detected by quant. RT-PCR anal. using an internal control template derived from multiple chemoresistance-related genes. Chemotherapy resistance can be mediated at several levels including the cell membrane (with drug exclusion or translocation out of cell), the nucleus (with altered expression of drug target), or metabolism (with increased metabolism of drug). Genes related to each of these three categories are the targets for RT-PCR evaluation in this invention. In order to allow simultaneous comparison of the gene expression levels within each category, an internal control template is created, containing both upstream (sense) and downstream (antisense) fragments from each gene in the category. Quant. RT-PCR anal. of human biol. samples is performed in the presence of the internal control and primers specific to each gene in the category. Expression level comparisons are made against a standard curve developed for real-time PCR. This multiple-gene

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anal. for detection of chemotherapeutic resistance is designed for tailoring cancer therapy to the individual, to reduce toxicity and increase efficacy.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:595201 HCAPLUS Full-text

DOCUMENT NUMBER: 139:333233

TITLE: Simple and sensitive high-performance liquid chromatography method for simultaneous determination of urinary free cortisol and 6 $\beta$ -hydroxycortisol in routine practice for CYP 3A4 activity evaluation in basal conditions and after grapefruit juice intake

AUTHOR(S): Rouits, E.; Boisdron-Celle, M.; Morel, A.; Gamelin, E.

CORPORATE SOURCE: CRLCC Paul Papin, Laboratoire d'Oncopharmacologie INSERM U564, Angers, 49100, Fr.

SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2003), 793(2), 357-366

CODEN: JCBAAI; ISSN: 1570-0232

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cytochrome P 450 3A4 activity displays a wide variability. The urinary 6 $\beta$ -hydroxycortisol to cortisol ratio, as a non-invasive assay, can be useful for its pretherapeutic characterization. The authors developed an HPLC-UV method preceded by liquid-liquid extraction for assessment of this ratio in clin. practice. Urine was collected on second void morning-spot sample. Percentage recoveries were high and reproducible. The 6 $\beta$ -hydroxycortisol to cortisol ratio ranged from 1.6 to 9.9 in 12 Caucasian healthy volunteers. It was reduced by 30 to 70% after ingestion of white grapefruit juice, a CYP3A4 inhibitor. The authors' method, simple, sensitive and accurate, could be helpful for determination of CYP 3A4 activity before oral chemotherapy, or for the monitoring of the use of grapefruit juice as a pharmacol. modulator.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:418688 HCAPLUS Full-text

DOCUMENT NUMBER: 136:160950

TITLE: A possible explanation for a neurotoxic effect of the anticancer agent oxaliplatin on neuronal voltage-gated sodium channels

AUTHOR(S): Grolleau, Francoise; Gamelin, Laurence; Boisdron-Celle, Michele; Lapied, Bruno; Pelhate, Marcel; Gamelin, Erick

CORPORATE SOURCE: Laboratoire de Neurophysiologie Unite Propre de Recherche de l'Enseignement Supérieur Equipe d'Accueil (UPRES EA) 2647, Université d'Angers, Unité de Formation et de Recherche (UFR) Sciences, Angers, F-49045, Fr.

SOURCE: Journal of Neurophysiology (2001), 85(5), 2293-2297

CODEN: JONEA4; ISSN: 0022-3077

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Oxaliplatin, a new widely used anticancer drug, displays frequent, sometimes severe, acute sensory neurotoxicity accompanied by neuromuscular signs that look like the symptoms observed in tetany and myotonia. The whole cell patch-clamp technique was employed to investigate the oxaliplatin effects on the electrophysiol. properties of short-term cultured dorsal unpaired median (DUM) neurons isolated from the CNS of the cockroach *Periplaneta americana*. Within the clin. concentration range, oxaliplatin (40-500  $\mu$ M), applied intracellularly, decreased the amplitude of the voltage-gated sodium current resulting in a reduction of half the amplitude of the action potential. For comparison, two other platinum derivs., cisplatin and carboplatin, were found to be ineffective at reducing the sodium current amplitude. In addition, we compared the oxaliplatin action to those of its metabolites dichloro-diaminocyclohexane platinum (dach-Cl<sub>2</sub>-platin) and oxalate. Oxalate (500  $\mu$ M) was found to be effective, like oxaliplatin, at reducing the inward sodium current amplitude, whereas dach-Cl<sub>2</sub>-platin (500  $\mu$ M) failed to change the current amplitude. Interestingly, the effect of oxalate or oxaliplatin could be mimicked by using intracellularly applied 10 mM bis-(o-aminophenoxy)-N,N,N',N'-tetraacetic acid (BAPTA), known as chelator of calcium ions. We concluded that oxaliplatin was capable of altering the voltage-gated sodium channels through a pathway involving calcium ions probably immobilized by its metabolite oxalate. The medical interest of preventing acute neurotoxic side effects of oxaliplatin by infusing Ca<sup>2+</sup> and Mg<sup>2+</sup> is discussed.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:619053 HCAPLUS Full-text

DOCUMENT NUMBER: 134:231567

TITLE: Docetaxel in combination with 5-fluorouracil in patients with metastatic breast cancer previously treated with anthracycline-based chemotherapy: a phase I, dose-finding study

AUTHOR(S): Lortholary, A.; Maillard, P.; Delva, R.; Boisdron-Celle, M.; Perard, D.; Vernillet, L.; Besenval, M.; Gamelin, E.

CORPORATE SOURCE: Centre Paul Papin, Angers, F-49033, Fr.

SOURCE: European Journal of Cancer (2000), 36(14), 1773-1780

CODEN: EJCAEL; ISSN: 0959-8049

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This phase I study evaluated the maximum tolerated dose, dose-limiting toxicity and recommended dose of docetaxel in combination with 5-fluorouracil (5-FU) in patients with metastatic breast cancer previously treated with anthracycline-based chemotherapy. Thirty-two patients received docetaxel at 60, 75, 85 or 100 mg/m<sup>2</sup> by 1-h i.v. infusion, followed, after a 1-h interval, by 5-FU at 250, 350, 500 or 750 mg/m<sup>2</sup>/day by continuous infusion over 5 days every 3 wk. Dose-limiting stomatitis defined the maximum tolerated dose at a docetaxel dose of 100 mg/m<sup>2</sup> with 5-FU at 750 mg/m<sup>2</sup>/day. None of 5 patients treated at the previous dose level (docetaxel 85 mg/m<sup>2</sup> with 5-FU 750 mg/m<sup>2</sup>/day) had a dose-limiting toxicity in the first cycle, and this was, therefore, considered the recommended dose. The combination was generally well tolerated. Grade 4 neutropenia was common (29 patients; 91%), but no patient experienced febrile neutropenia of duration >3 days requiring i.v. antibiotics. An objective response was achieved by 18 patients overall (56%), and in 4 of 5 patients treated with the determined recommended dose. No pharmacokinetic interaction between docetaxel and 5-FU was apparent.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS

L74 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:757636 HCAPLUS Full-text

DOCUMENT NUMBER: 134:50966

TITLE: Early biotransformations of oxaliplatin after its intravenous administration to cancer patients

AUTHOR(S): Allain, Pierre; Heudi, Oliver; Cailleux, Annie; Le Bouil, Anne; Larra, Francis; Boisdron-Celle, Michele; Gamelin, Erik

CORPORATE SOURCE: Laboratoire de Pharmacologie et Toxicologie, Centre Hospitalier Universitaire, Angers, 49033, Fr.

SOURCE: Drug Metabolism and Disposition (2000), 28(11), 1379-1384

CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This article deals with the fate of oxaliplatin 1 and 3 h after its i.v. administration (130 mg/m<sup>2</sup>) to three patients. Its binding to plasma proteins and penetration into red blood cells were monitored by chromatog. online with inductively coupled plasma mass spectrometry. Oxaliplatin biotransformations in plasma ultrafiltrate (PUF) and in urine were studied by chromatog. coupled to inductively coupled plasma mass spectrometry or to electrospray ionization mass spectrometry. In plasma, four platinum (Pt) compds. were found. The peaks at 200 and 160 kDa corresponding to  $\gamma$ -globulins contained 40% of the Pt bound; the peak at 60 kDa corresponding to albumin contained 40% of the Pt found. The peak <2 kDa could correspond to oxaliplatin, to its degradation products, or to adducts between Pt compds. and low-mol.-weight species such as glutathione, L-methionine, and L-cysteine. In PUF and urine, oxaliplatin itself, its degradation products, Pt(dach)Cl<sub>2</sub>, [Pt(dach)(OH<sub>2</sub>)Cl]<sup>+</sup>, and species that have the same retention times as Pt(dach)(methionine) and [Pt(dach)]<sub>2</sub>(glutathione) were found. One hour after infusion, oxaliplatin in PUF and urine represented 12 and 50% of the total Pt, resp. Three hours after infusion, oxaliplatin, undetectable in PUF, represented 10% of total Pt in urine. Inside red blood cells, two Pt compds. were found. The Pt peak at 60 kDa corresponding to Hb and the peak <2 kDa corresponding to low-mol. species contained, resp., 60% and 40% of Pt found. This study demonstrates that in the first hours after its infusion, oxaliplatin, in addition to other Pt compds., is present in plasma and urine and that Pt is bound to albumin,  $\gamma$ -globulins, and Hb.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:717375 HCAPLUS Full-text

DOCUMENT NUMBER: 134:275301

TITLE: Dose and time dependencies of 5-fluorouracil pharmacokinetics

AUTHOR(S): Terret, Catherine; Erdociain, Eric; Guimbaud, Rosine; Boisdron-Celle, Michele; McLeod, Howard L.; Fety-Deporte, Regine; Lafont, Thierry; Gamelin, Erick; Bugat, Roland; Canal, Pierre; Chatelut, Etienne

CORPORATE SOURCE: Institut Claudius-Regaud and Universite Paul-Sabatier, Toulouse, Fr.

SOURCE: Clinical Pharmacology &amp; Therapeutics (St. Louis) (2000), 68(3), 270-279

CODEN: CLPTAT; ISSN: 0009-9236

PUBLISHER: Mosby, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Objectives: The purpose of this study was to examine the interpatient and inpatient variability of the Michaelis-Menten plasma parameters of 5-fluorouracil administered according to a schedule combining a bolus of 400 mg/m<sup>2</sup> followed by 22-h infusion of 600 mg/m<sup>2</sup> for 2 consecutive days. Patients: A pharmacokinetic population approach was used to analyze the data from 21 patients with colorectal cancer. Results: The 5-fluorouracil plasma concns. vs. time were best described by a two-compartment model with nonlinear elimination from the central compartment. The relationships between the pharmacokinetic parameters and patient characteristics were tested. On day 1 the mean values (with interindividual variability as expressed by the coefficient of variation) were 1390 mg · h<sup>-1</sup> (20%), and 5.57 mg · L<sup>-1</sup> (22%) for the maximum rate of elimination, and the half-saturating plasma concentration. The maximum rate of elimination was pos. correlated to the body surface area and the percentage of liver involvement by metastatic disease determined by tomodesitometric examination. The model was successfully tested with independent data sets corresponding to other schedules. The anal. of this inpatient variability showed that the half-saturating plasma concentration increased from day 1 to day 2, especially in the patients with low lymphocyte cell dihydropyrimidine dehydrogenase activity. Conclusion: The pharmacokinetic parameters obtained in this study would be useful to predict the 5-fluorouracil plasma concns. following other schedules of administration of 5-fluorouracil and to study the possible pharmacokinetic interactions between 5-fluorouracil and other drugs.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:253473 HCAPLUS Full-text

DOCUMENT NUMBER: 130:306010

TITLE: Correlation between uracil and dihydrouracil plasma ratio, fluorouracil (5-FU) pharmacokinetic parameters, and tolerance in patients with advanced colorectal cancer: a potential interest for predicting 5-FU toxicity and determining optimal 5-FU dosage

AUTHOR(S): Gamelin, E.; Boisdron-Celle, M.; Guerin-Meyer, V.; Delva, R.; Lortholary, A.; Genevieve, F.; Larra, F.; Ifrah, N.; Robert, J.

CORPORATE SOURCE: Departement d'Oncologie Medicale and d'Oncopharmacologie, Centre Paul Papin, Angers, 49033, Fr.

SOURCE: Journal of Clinical Oncology (1999), 17(4), 1105-1110

CODEN: JCONDN; ISSN: 0732-183X

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Patients with genetic fluorouracil (5-FU) catabolic deficiencies are at high risk for severe toxicity. To predict 5-FU catabolic deficiencies and toxic side effects, we conducted a prospective study of patients treated for advanced colorectal cancer by high-dose 5-FU. Eighty-one patients were treated with weekly infusions of 5-FU and folinic acid. The initial 5-FU dose of 1,300 mg/m<sup>2</sup> was individually adjusted according to a dose-adjustment chart. Plasma concns. of uracil (U) and its dihydrogenated metabolite, dihydrouracil (UH<sub>2</sub>), were measured before treatment, and the ratio of UH<sub>2</sub> to U was calculated. Pharmacokinetic and pharmacodynamic studies were conducted to look for a relationship between the ratio of UH<sub>2</sub> to U and 5-FU metabolic outcome and tolerance. The UH<sub>2</sub>-U ratios were normally distributed (mean value, 2.82;

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range, 0.35 to 7.13) and were highly correlated to (1) 5-FU plasma levels after the first course of treatment ( $r = .58$ ), (2) 5-FU plasma clearance ( $r = .639$ ), and (3) individual optimal therapeutic 5-FU dose ( $r = .65$ ). Toxic side effects were observed only in patients with initial UH2-U ratios of less than 1.8. No adverse effects were noted in patients with UH2-U ratios of greater than 2.25. The UH2-U ratio, easily determined before treatment, could help to identify patients with metabolic deficiency and, therefore, a risk of toxicity.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:265236 HCAPLUS Full-text

DOCUMENT NUMBER: 129:12401

TITLE: Long-term weekly treatment of colorectal metastatic cancer with fluorouracil and leucovorin: results of a multicentric prospective trial of fluorouracil dosage optimization by pharmacokinetic monitoring in 152 patients

AUTHOR(S): Gamelin, E.; Boisdron-Celle, M.; Delva, R.; Regimbeau, C.; Cailleux, P. E.; Alleaume, C.; Maillet, M. L.; Goudier, M. J.; Sire, M.; Person-Joly, M. C.; Maigre, M.; Maillart, P.; Fety, R.; Burtin, P.; Lortholary, A.; Dumesnil, Y.; Picon, L.; Geslin, J.; Gesta, P.; Danquechin-Dorval, E.; Larra, F.; Robert, J.

CORPORATE SOURCE: Service d'Oncologie Medicale et de Pharmacologie Clinique, Centre Paul Papin, Angers, 49033, Fr.

SOURCE: Journal of Clinical Oncology (1998), 16(4), 1470-1478

CODEN: JCONDN; ISSN: 0732-183X

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Therapeutic intensification of 5-fluorouracil (5-FU) with individual dose adjustment was studied in a multicentric phase II prospective trial. Weekly high-dose 5-FU was administered by 8-h infusion with 400 mg leucovorin/m<sup>2</sup>. The initial dose of 5-FU (1300 mg/m<sup>2</sup>) was adjusted weekly according to plasma 5-FU levels, to reach the therapeutic range previously determined. Toxicity was mainly diarrhea (39%, with 5% grade 3) and hand-foot syndrome (30%, with 2% grade 3). Among 117 patients with measurable disease, 18 had a complete response, 48 a partial response, 35 a minor response and stable disease, and 16 progressive disease. Median overall survival time was 19 mo. The therapeutic plasma 5-FU range was rapidly reached with a variable 5-FU dose in the patient population: mean, 1803 mg/m<sup>2</sup>/wk (range, 950-3396). Thirteen patients were immediately in the toxic dose zone, whereas 51 required a ≥50% dose increase. Thus, individual 5-FU dose adjustment with pharmacokinetic monitoring provided a high survival rate and percentage of responses, with good tolerance.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:276451 HCAPLUS Full-text

DOCUMENT NUMBER: 129:12244

TITLE: Determination of unbound platinum after oxaliplatin administration: comparison of currently available methods and influence of various parameters

AUTHOR(S): Gamelin, E.; Boisdron-Celle, M.; Lebouil, A.; Turcant, A.; Cailleux, A.; Krikorian, A.;



Brienza, S.; Cvitkovic, E.; Larra, F.; Robert, J.; Allain, P.  
 CORPORATE SOURCE: Dep. Medical Oncology & Clinical Pharmacology, Centre Pual-Papin, Centre Regional Lutte Contre Cancer, Angers, 49033, Fr.  
 SOURCE: Anti-Cancer Drugs (1998), 9(3), 223-228  
 CODEN: ANTDEV; ISSN: 0959-4973  
 PUBLISHER: Rapid Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Variations in plasma protein binding may have profound effects on both disposition and activity of drugs, especially for those which are tightly bound to proteins, such as anticancer platinum derivs. Methods of separation of the non-protein-bound fraction and some tech. parameters may influence the results. We have compared ultrafiltration and ultracentrifugation, as well as the effect of potentially interfering factors, upon the determination of the plasma unbound platinum fraction after oxaliplatin administration to cancer patients. Ultrafiltration and ultracentrifugation provided very closely correlated results, so that either technique can be used. The ultrafiltration cut-off (3000-30 000 Da) devices, the type of tube for blood sampling and the type of anticoagulant (none, lithium heparinate or EDTA) did not influence the results markedly. In contrast, results were greatly influenced by freezing: erratic results were obtained on thawed plasma when compared with those on fresh serum or plasma. Consequences may be important in usual practice, since many pharmacokinetic studies are carried out in multicentric trials with plasma processing centralized in one reference laboratory. The methods for the determination of protein-drug binding should be standardized and guidelines elaborated where optimal conditions for each type of binding assay are given.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:714446 HCAPLUS Full-text  
 DOCUMENT NUMBER: 127:355014  
 TITLE: A simple chromatographic method for the analysis of pyrimidines and their dihydrogenated metabolites  
 AUTHOR(S): Gamelin, E.; Boisdron-Celle, M.; Larra, F.; Robert, J.  
 CORPORATE SOURCE: Laboratoire d'Oncopharmacologie, Centre Paul-Papin, Angers, 49033, Fr.  
 SOURCE: Journal of Liquid Chromatography & Related Technologies (1997), 20(19), 3155-3172  
 CODEN: JLCTFC; ISSN: 1082-6076  
 PUBLISHER: Dekker  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB A simple, sensitive and accurate liquid-chromatog. method was developed for the simultaneous determination of uracil, 5-fluorouracil and their dihydrogenated metabolites in plasma. This method offers a useful tool for the detection of defects in pyrimidine degradation. HPLC was carried out on serial Spherisorb ODS1 (10-cm) and ODS2 (25-cm) columns, with 10 mM phosphate buffer, pH 3.0, as the mobile phase and UV detection at 205 nm. Many parameters, such as mobile phase pH, ionic strength, and column temperature, had a marked influence on the results. The ratio dihydrouracil/uracil was calculated, and a Gaussian distribution of this ratio was found in a population of healthy volunteers.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

10/501318

ACCESSION NUMBER: 1997:427217 HCAPLUS Full-text  
DOCUMENT NUMBER: 127:103877  
TITLE: Cumulative pharmacokinetic study of oxaliplatin,  
administered every three weeks, combined with  
5-fluorouracil in colorectal cancer patients  
AUTHOR(S): Gamelin, erick; Le Bouil, Anne;  
Boisdron-Celle, Michele; Turcant, Alain;  
Delva, Remy; Cailleux, Annick; Krikorian, Anais;  
Brienza, Silvano; Cvitkovic, Esteban; Robert, Jacques;  
Larra, Francis; Allain, Pierre  
CORPORATE SOURCE: Department of Medical Oncology and Clinical  
Pharmacology, Centre Paul Papin, Centre Regional de  
Lutte Contre le Cancer, Angers, 49033, Fr.  
SOURCE: Clinical Cancer Research (1997), 3(6),  
891-899  
CODEN: CCREF4; ISSN: 1078-0432  
PUBLISHER: American Association for Cancer Research  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The cumulative pharmacokinetic pattern of oxaliplatin, a new  
diamminecyclohexane platinum derivative, was studied in patients with  
metastatic colorectal cancer. Oxaliplatin was administered by i.v. infusion  
(130 mg/M2) over 2 h every 3 wk, and 5-fluorouracil and leucovorin were  
administered weekly. A very sensitive method, inductively coupled plasma-mass  
spectrometry, allowed for the determination of total plasma and  
ultracentrifugable (UC) and RBC platinum levels on day 1, at 0, 2, and 5 h,  
and on days 8, 15, and 22. Sixteen patients underwent three or more courses,  
and six of them underwent six or more courses. The platinum concentration  
curves were quite similar from one course to another, with a high peak value 2  
h after administration (day 1, Cmax = 3201±609 µg/L) and a rapid decrease (day  
8, 443±99 µg/L). Cmax of both total and UC platinum levels in plasma remained  
unchanged throughout the treatment. The mean total platinum half-life in  
plasma was 9 days. The authors found residual levels of total platinum on day  
22 (161±45 µg/L), but the authors observed no significant accumulation for the  
four first cycles (P = 0.57). In contrast, platinum accumulated significantly  
in RBCs after three courses (+91% at day 22 of the third cycle vs. day 22 of  
the first cycle, P = 0.000018), and its half-life there was equivalent to that  
of RBCs. The patterns of UC and total platinum concentration curves were very  
similar and correlated significantly (P < 10-6) at all sampling times. The  
mean UC:total platinum ratio was 15% at day 1 and 5% at days 8, 15, and 22 in  
the 3-wk treatment course. Unlike cisplatin, which rapidly accumulates in  
plasma as both free and bound platinum, oxaliplatin does not accumulate in  
plasma, but it does accumulate in RBCs, after repeated cycles at the currently  
recommended dose (130 mg/M2) and schedule of administration (every 3 wk).  
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 1997:469684 HCAPLUS Full-text  
DOCUMENT NUMBER: 127:185285  
TITLE: Rapid and sensitive high-performance liquid  
chromatographic analysis of halogenopyrimidines in  
plasma  
AUTHOR(S): Gamelin, E.; Boisdron-Celle, M.;  
Turcant, A.; Larra, F.; Allain, P.; Robert, J.  
CORPORATE SOURCE: Laboratory of Pharmacology, Centre Paul Papin, 2 Rue  
Moll, Angers, 49000, Fr.  
SOURCE: Journal of Chromatography, B: Biomedical Sciences and  
Applications (1997), 695(2), 409-416

10/501318

CODEN: JCBBEP; ISSN: 0378-4347

PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Recent studies have stressed the need for individual adjustment of 5-fluorouracil (5-FU) dosage. Most of the techniques previously reported are not well adapted to routine application. We describe a sensitive, selective and simple HPLC technique under isocratic conditions for the quantitation of 5-FU and other halogenopyrimidines. The proportion of reagents and internal standard were optimized to allow the use of minitubes, particularly adapted to large series of plasma assays. High extraction yield, 75% for 5-FU and 90% for 5-bromouracil and 5-chlorouracil, was obtained using 1.2 mL isopropanol-Et acetate (15:85, volume/volume) following precipitation of plasma proteins with 300 mg ammonium sulfate. The mobile phase was 0.01 M phosphate buffer (pH 3.0). Uracil and 5-fluorouracil were fully resolved with Spherisorb ODS2 column. The limits of quantitation and detection in human plasma were 6 ng mL<sup>-1</sup> and 3 ng mL<sup>-1</sup>, resp., for all compds. studied. The total anal. time required for each run was 25 min. Final results could be given within 90 min of blood sampling. At least 50 plasma samples could be analyzed per day. This method has been successfully used for monitoring 5-FU-based treatments.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 14-19 ibib ab

L74 ANSWER 14 OF 19 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2007183629 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 17064846  
TITLE: 5-Fluorouracil-related severe toxicity: a comparison of different methods for the pretherapeutic detection of dihydropyrimidine dehydrogenase deficiency.  
AUTHOR: Boisdron-Celle M; Remaud G; Traore S; Poirier A  
L; Gamelin L; Morel A; Gamelin E  
CORPORATE SOURCE: Oncopharmacology and Pharmacogenetic Laboratory, INSERM U564, Centre Paul Papin, 2 rue Moll, 49933 Angers cedex 9, France.  
SOURCE: Cancer letters, (2007 May 8) Vol. 249, No. 2, pp. 271-82.  
Electronic Publication: 2006-10-24.  
Journal code: 7600053. ISSN: 0304-3835.  
PUB. COUNTRY: Ireland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200706  
ENTRY DATE: Entered STN: 28 Mar 2007  
Last Updated on STN: 5 Jun 2007  
Entered Medline: 4 Jun 2007

AB 5-Fluorouracil (5-FU)-related early toxicity, due to a metabolic deficiency, is rare but is potentially severe and even lethal (0.1%). It is due to dihydropyrimidine dehydrogenase (DPYD) gene polymorphism or some epigenetic factors. The detection of metabolic change could prevent severe toxicity, but until now it has not been carried out in clinical practice. PURPOSE: To find the simplest and most accurate pretherapeutic test to predict DPD deficiency in patients treated with 5-FU by comparing different approaches. RESULTS: Two hundred and fifty two French Caucasian patients treated by 5-FU infusion were studied. A two-step strategy, combining firstly SNP detection and uracil plasma measurement, followed, in cases where metabolic deficiency was

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suspected, by dihydrouracil/uracil ratio determination to confirm deficiency and to determine the optimum 5-FU dosage, appeared the best approach, with 83% and 82% sensitivity and specificity, respectively. CONCLUSION: These data support the future use of this approach, suitable to clinical practice, as screening test to identify DPD deficiency before 5-FU-based therapy.

L74 ANSWER 15 OF 19 MEDLINE on STN DUPLICATE 3  
ACCESSION NUMBER: 2004316128 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 15217938  
TITLE: Prevention of oxaliplatin-related neurotoxicity by calcium and magnesium infusions: a retrospective study of 161 patients receiving oxaliplatin combined with 5-Fluorouracil and leucovorin for advanced colorectal cancer.  
AUTHOR: Gamelin Laurence; Boisdron-Celle Michele  
; Delva Remy; Guerin-Meyer Veronique; Ifrah Norbert;  
Morel Alain; Gamelin Erick  
CORPORATE SOURCE: Department of Medical Oncology and Oncopharmacology, INSERM U564, Anticancer Centre Paul Papin, Angers Cedex, France.  
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (2004 Jun 15)  
Vol. 10, No. 12 Pt 1, pp. 4055-61.  
Journal code: 9502500. ISSN: 1078-0432.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200501  
ENTRY DATE: Entered STN: 26 Jun 2004  
Last Updated on STN: 4 Jan 2005  
Entered Medline: 3 Jan 2005  
AB PURPOSE: Oxaliplatin is active in colorectal cancer. Sensory neurotoxicity is its dose-limiting toxicity. It may come from an effect on neuronal voltage-gated Na channels, via the liberation one its metabolite, oxalate. We decided to use Ca and Mg as oxalate chelators. EXPERIMENTAL DESIGN: A retrospective cohort of 161 patients treated with oxaliplatin + 5-fluorouracil and leucovorin for advanced colorectal cancer, with three regimens of oxaliplatin (85 mg/m(2)/2w, 100/2w, 130/3w) was identified. Ninety-six patients received infusions of Ca gluconate and Mg sulfate (1 g) before and after oxaliplatin (Ca/Mg group) and 65 did not. RESULTS: Only 4% of patients withdrew for neurotoxicity in the Ca/Mg group versus 31% in the control group (P = 0.000003). The tumor response rate was similar in both groups. The percentage of patients with grade 3 distal paresthesia was lower in Ca/Mg group (7 versus 26%, P = 0.001). Acute symptoms such as distal and lingual paresthesia were much less frequent and severe (P = 10(-7)), and pseudolaryngospasm was never reported in Ca/Mg group. At the end of the treatment, 20% of patients in Ca/Mg group had neuropathy versus 45% (P = 0.003). Patients with grade 2 and 3 at the end of the treatment in the 85 mg/m(2) oxaliplatin group recovered significantly more rapidly from neuropathy than patients without Ca/Mg. CONCLUSIONS: Ca/Mg infusions seem to reduce incidence and intensity of acute oxaliplatin-induced symptoms and might delay cumulative neuropathy, especially in 85 mg/m(2) oxaliplatin dosage.

L74 ANSWER 16 OF 19 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 4  
ACCESSION NUMBER: 2002:408722 BIOSIS Full-text  
DOCUMENT NUMBER: PREV200200408722  
TITLE: Oxaliplatin neurotoxicity: Pathogenic mechanism and

therapeutic approach.

AUTHOR(S): Gamelin, Laurence [Reprint author];  
Boisdron-Celle, Michele [Reprint author]; Craipeau,  
Marie-Claire [Reprint author]; Morel, Alain  
[Reprint author]; Gamelin, Erick [Reprint author]

CORPORATE SOURCE: CRLCC Paul Papin, Angers, France

SOURCE: Proceedings of the American Association for Cancer Research  
Annual Meeting, (March, 2002) Vol. 43, pp. 492. print.  
Meeting Info.: 93rd Annual Meeting of the American  
Association for Cancer Research. San Francisco, California,  
USA. April 06-10, 2002.  
ISSN: 0197-016X.

DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 31 Jul 2002  
Last Updated on STN: 23 Sep 2002

L74 ANSWER 17 OF 19 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2006:584637 BIOSIS Full-text

DOCUMENT NUMBER: PREV200600595263

TITLE: Involvement of the steroid and xenobiotic receptor SXR in  
irinotecan resistance.

AUTHOR(S): Basseville, Agnes [Reprint Author]; Gamelin,  
Laurence; Boisdron-Celle, Michele; Coqueret,  
Olivier; Gamelin, Erick; Morel, Alain

CORPORATE SOURCE: CRLCC Paul Papin, Angers, France

SOURCE: Proceedings of the American Association for Cancer Research  
Annual Meeting, (APR 2006) Vol. 47, pp. 298-299.  
Meeting Info.: 97th Annual Meeting of the  
American-Association-for-Cancer-Research (AACR).  
Washington, DC, USA. April 01 -05, 2006. Amer Assoc Canc  
Res.  
ISSN: 0197-016X.

DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 8 Nov 2006  
Last Updated on STN: 8 Nov 2006

L74 ANSWER 18 OF 19 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights  
reserved on STN

ACCESSION NUMBER: 2006169851 EMBASE Full-text

TITLE: [Oxaliplatin neurotoxicity].  
NEUROTOXICITE DE L'OXALIPLATINE.

AUTHOR: Gamelin L.; Boisdron-Celle M.;  
Morel A.; Gamelin E.

CORPORATE SOURCE: L. Gamelin, Service de Toxicologie, Centre Antipoisons, CHU  
Angers, Angers, France

SOURCE: Bulletin du Cancer, (2006) Vol. 93, No. SPEC. ISS., pp.  
S17-S22. .  
Refs: 26  
ISSN: 0007-4551 E-ISSN: 1769-6917 CODEN: BUCABS

COUNTRY: France

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer  
037 Drug Literature Index  
038 Adverse Reactions Titles  
048 Gastroenterology

10/501318

LANGUAGE: French  
SUMMARY LANGUAGE: English; French  
ENTRY DATE: Entered STN: 28 Apr 2006  
Last Updated on STN: 28 Apr 2006

AB Oxaliplatin is a reference drug in the treatment of digestive-tract tumors, especially colorectal cancer. Its toxicity profile is dominated by a peripheral sensitive neuropathy, with neuromuscular manifestations. This neurotoxicity has 2 components: an acute toxicity characterized by a rapid onset of cold-induced distal dysesthesia and/or paresthesia, muscular contractions, numbness, stiffness, usually transient but able to evolve into a chronic, persistent sensory peripheral neuropathy that eventually causes functional impairment. A persistent sensory peripheral neuropathy may develop with prolonged treatment, eventually causing superficial and deep sensory loss, sensory ataxia and functional impairment. This neurotoxicity is frequent, 80% of the patients and becomes chronic in 15 to 20% of the patients, sometimes irreversible. The mechanism of this neurotoxicity has been elucidated: an increased neuronal excitability is due to the action of oxaliplatin on voltage-gated sodium channels through chelation of calcium by the oxaliplatin metabolite. The prevention of this neurotoxicity is a major goal, taking in account the wide indications of this drug. Different approaches have been or are evaluated, based on pathogenic or practical concepts: 1) modifications of the administration schedule; 2) substances acting upon sodium channels: calcium-magnesium, carbamazepine, gabapentine, venlafaxin; 3) detoxifying agents and antioxidants: glutathione, amifostine,  $\alpha$ -lipoic acid, tocopherol; 4) substances used in other kinds of neuropathy: glutamine,  $\alpha$ -lipoic acid; 5) neurotrophic factors: NGF, LIF; 6) oxaliplatin analogs, with a DACH platin, without oxalate. Calcium-magnesium infusion seems to be an efficient and safe approach. Further studies are necessary for a better understanding and prevention of this neurotoxicity, potentially severe.  
.COPYRGHT. John Libbey Eurotext.

L74 ANSWER 19 OF 19 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN  
ACCESSION NUMBER: 2006-40952 DRUGU P Full-text  
TITLE: Involvement of the steroid and xenobiotic receptor SXR in  
irinotecan resistance.  
AUTHOR: Basseville A; Gamelin L; Boisdron-Celle M  
; Coqueret O; Gamelin E; Morel A  
LOCATION: Angers, France  
SOURCE: Proc.Am.Assoc.Cancer Res. (47, Abs1264, 2006) 0 Ref.  
ISSN: 0197-016X  
AVAIL. OF DOC.: CRLCC Paul Papin, Angers, France.  
LANGUAGE: English  
DOCUMENT TYPE: Journal  
FIELD AVAIL.: AB; LA; CT  
FILE SEGMENT: Literature

AB The role of steroid and xenobiotic receptor (SX) in irinotecan (IT) resistance was evaluated in LS180 cells. SX when activated by IT or SN-38, induced cytochrome P450 3A4, partially responsible for IT inactivation and p21waf1. Cell cycle arrest, coupled to detoxification, would allow the cells to repair DNA damages induced by chemotherapy. The Authors try to inhibit SX by siRNA during IT/SN-38 treatment to observe the impact upon drug cytotoxicity. Given that SX can be activated by cytotoxic drugs paclitaxel (Taxol) or cisplatin and can regulate a broad range of detoxification genes, the nuclear receptor is an ideal molecular target for the manipulation of this detoxification network. (conference abstract: 97th Annual Meeting of the American Association for Cancer Research, Washington, DC, USA, 01/04/2006-05/04/2006)

## \*\*\*\*\* INVENTOR RESULTS \*\*\*\*\*

=&gt; d his 142

(FILE 'HCAPLUS' ENTERED AT 09:02:52 ON 04 AUG 2007)

L42 13 S L38 AND L41

=&gt; d que 142

L2 11 SEA FILE=REGISTRY ABB=ON PLU=ON (10043-52-4/BI OR 11116-97-5/BI OR 135701-98-3/BI OR 144-62-7/BI OR 299-28-5/BI OR 33659-28-8/BI OR 471-34-1/BI OR 61825-94-3/BI OR 7439-95-4/BI OR 7440-70-2/BI OR 7487-88-9/BI)

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L4 1 SEA FILE=REGISTRY ABB=ON PLU=ON OXALIPLATIN/CN

L6 1 SEA FILE=REGISTRY ABB=ON PLU=ON OXALIC ACID/CN

L7 1 SEA FILE=REGISTRY ABB=ON PLU=ON 144-62-7/RN

L8 2 SEA FILE=REGISTRY ABB=ON PLU=ON L3 OR L4 OR L6 OR L7

L9 9 SEA FILE=REGISTRY ABB=ON PLU=ON L2 NOT L8

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L11 QUE ABB=ON PLU=ON OXALIPLATIN

L14 QUE ABB=ON PLU=ON CANCER? OR NEOPLAS? OR TUMOR? OR TUMOUR?

L15 QUE ABB=ON PLU=ON ANTIVIRAL? OR ANTI(W)VIRAL? OR VIRUS? OR ANTIVIRUS? OR ANTI(W)VIRUS?

L16 QUE ABB=ON PLU=ON ?VIRUS? OR ?VIRAL?

L17 QUE ABB=ON PLU=ON NEUROTOXIC?

L22 QUE ABB=ON PLU=ON AY<2004 OR PY<2004 OR PRY<2004 OR MY<2004 OR REVIEW/DT

L24 56622 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 OR L11

L25 62777 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 OR L24

L26 623520 SEA FILE=HCAPLUS ABB=ON PLU=ON L9

L27 110313 SEA FILE=HCAPLUS ABB=ON PLU=ON CALCIUM/OBI (2A) (GLUCONATE/OBI OR CHLORIDE/OBI OR BROMOGALACTOGLUCONATE/OBI OR CARBONATE/OBI)

L28 19480 SEA FILE=HCAPLUS ABB=ON PLU=ON MAGNESIUM/OBI (2A) (SULFATE/OBI OR PIDOLATE/OBI)

L29 635324 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 OR L28 OR L26

L30 4522 SEA FILE=HCAPLUS ABB=ON PLU=ON L25 AND L29

L31 59 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND L14

L32 37 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND (L15 OR L16)

L33 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND L17

L34 82 SEA FILE=HCAPLUS ABB=ON PLU=ON L31 OR L32 OR L33

L36 67 SEA FILE=HCAPLUS ABB=ON PLU=ON L34 AND L22

L37 1444895 SEA FILE=HCAPLUS ABB=ON PLU=ON 1/SC, SX

L38 38 SEA FILE=HCAPLUS ABB=ON PLU=ON L36 AND L37

L41 254740 SEA FILE=HCAPLUS ABB=ON PLU=ON INJECT?/OBI OR ORAL?/OBI

L42 13 SEA FILE=HCAPLUS ABB=ON PLU=ON L38 AND L41

=&gt; d his 170

(FILE 'MEDLINE, BIOSIS, EMBASE, BIOTECHNO, DRUGU' ENTERED AT 09:14:57 ON 04 AUG 2007)

L70 9 S L69 AND L22

=&gt; d que 170

L10 QUE ABB=ON PLU=ON OXALATE OR OXALIC ACID

L11 QUE ABB=ON PLU=ON OXALIPLATIN

L13 QUE ABB=ON PLU=ON MAGNESIUM (2A) (SULFATE OR PIDOLATE)

L14 QUE ABB=ON PLU=ON CANCER? OR NEOPLAS? OR TUMOR? OR TUM

10/501318

OUR?  
L15 QUE ABB=ON PLU=ON ANTIVIRAL? OR ANTI(W)VIRAL? OR VIRUS  
? OR ANTIVIRUS? OR ANTI(W)VIRUS?  
L16 QUE ABB=ON PLU=ON ?VIRUS? OR ?VIRAL?  
L17 QUE ABB=ON PLU=ON NEUROTOXIC?  
L22 QUE ABB=ON PLU=ON AY<2004 OR PY<2004 OR PRY<2004 OR MY  
<2004 OR REVIEW/DT  
L24 56622 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 OR L11  
L27 110313 SEA FILE=HCAPLUS ABB=ON PLU=ON CALCIUM/OBI (2A) (GLUCONATE/OB  
I OR CHLORIDE/OBI OR BROMOGALACTOGLUCONATE/OBI OR CARBONATE/OBI  
)  
L28 19480 SEA FILE=HCAPLUS ABB=ON PLU=ON MAGNESIUM/OBI (2A) (SULFATE/OB  
I OR PIDOLATE/OBI)  
L39 1286494 SEA FILE=HCAPLUS ABB=ON PLU=ON (TREAT#/OBI OR TREATMENT#/OBI  
OR PREVENT#/OBI OR CURE#/OBI)  
L41 254740 SEA FILE=HCAPLUS ABB=ON PLU=ON INJECT#/OBI OR ORAL#/OBI  
L56 52321 SEA L24  
L57 61889 SEA L27  
L58 18226 SEA L28  
L59 78565 SEA L57 OR L58  
L60 947 SEA L56 AND L59  
L61 53 SEA L60 AND L14  
L62 5 SEA L60 AND L15  
L63 10 SEA L60 AND L16  
L64 25 SEA L60 AND L17  
L65 63 SEA (L61 OR L62 OR L63 OR L64)  
L66 42 SEA L39 AND L65  
L67 25 SEA L41 AND L65  
L68 47 SEA L66 OR L67  
L69 17 SEA L68 NOT L13  
L70 9 SEA L69 AND L22

=> dup rem 142 170

PROCESSING COMPLETED FOR L42

PROCESSING COMPLETED FOR L70

L75 21 DUP REM L42 L70 (1 DUPLICATE REMOVED)  
ANSWERS '1-13' FROM FILE HCAPLUS  
ANSWER '14' FROM FILE MEDLINE  
ANSWER '15' FROM FILE BIOSIS  
ANSWERS '16-18' FROM FILE EMBASE  
ANSWERS '19-21' FROM FILE DRUGU

=> d 1-13 ibib ed ab hitind

L75 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:149000 HCAPLUS Full-text

DOCUMENT NUMBER: 144:219302

TITLE: Composition comprising mixture of ubiquinones, lactic  
acid dehydrogenase inhibitor, compound capable of  
augmenting oxidative phosphorylation and compound that  
antagonize gluconeogenesis from non-glucose carbon  
based substrates for treatment of cancer

INVENTOR(S): Mazzio, Elizabeth Anne; Soliman, Karam F.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.--in-part of U.S.  
Ser. No. 909,590, abandoned.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English



FAMILY ACC. NUM. COUNT: 2

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006035981	A1	20060216	US 2005-233279	20050920 <--
PRIORITY APPLN. INFO.:			US 2003-491841P	P 20030802 <--
			US 2004-540525P	P 20040129
			US 2004-909590	B2 20040802

ED Entered STN: 17 Feb 2006

AB This invention discloses a method and formulation for treatment/prevention of human and animal cancers. The invention is designed to exploit the vulnerability of cancer with regards to its anaerobic requirement for non-oxidative phosphorylation of glucose to derive energy, which is opposite to the host. The composition is comprised of a combination of one or more of (A) 2,3-dimethoxy-5-methyl-1,4-benzoquinone, ubiquinones (B) compound(s) capable of augmenting oxidative phosphorylation such as a riboflavin containing compound and/or ubiquinone (C) 2',3,4,5,7- pentahydroxyflavone or a lactic acid dehydrogenase inhibitor and (D) compds. (s) that antagonize gluconeogenesis from non-glucose carbon based substrates. The combination of these substances should favor oxidative loss of carbon through decarboxylation reactions, suppress gluconeogenesis and initiate collapse of glycolysis in tumor tissue, a chemical manipulation that should be non-toxic or perhaps even beneficial to normal respiring host tissue. Pilot studies indicate the treatment to be effective without side effects.

INCL 514690000; 514045000; 514051000; 514027000; 514251000; 424725000;  
424748000; 424756000; 424745000; 424746000

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

IT Lymphoma

(Burkitt's; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Drug delivery systems

(aerosols; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Neuroglia, neoplasm

(astrocytoma; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Tea products

(beverages, green; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Drug delivery systems

(capsules; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Uterus, neoplasm

(cervix; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

- IT Intestine, neoplasm  
 (colon; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Acute lymphocytic leukemia  
 Acute myeloid leukemia  
 Adrenal gland, neoplasm  
 Antitumor agents  
 Antitumor agents  
 Bile duct, neoplasm  
 Binders  
 Bladder, neoplasm  
 Bone, neoplasm  
 Brain, neoplasm  
 Bronchi, neoplasm  
 Carcinoma  
 Central nervous system, neoplasm  
 Combination chemotherapy  
 Digestive tract, neoplasm  
 Electrolytic solutions  
 Emulsifying agents  
 Eye, neoplasm  
 Fillers  
 Foaming agents  
 Gallbladder, neoplasm  
 Gluconeogenesis  
 Head and Neck, neoplasm  
 Hematopoietic neoplasm  
 Hodgkin's disease  
 Humectants  
 Kidney, neoplasm  
 Liver, neoplasm  
 Lung, neoplasm  
 Lymphoma  
 Mammary gland, neoplasm  
 Mouth, neoplasm  
 Myristica  
 Neuroglia, neoplasm  
 Nose, neoplasm  
 Ovary, neoplasm  
 Oxidative phosphorylation, biological  
 Pancreas, neoplasm  
 Parathyroid gland, neoplasm  
 Pituitary gland, neoplasm  
 Prostate gland, neoplasm  
 Rosmarinus officinalis  
 Skin, neoplasm  
 Stomach, neoplasm  
 Surfactants  
 Syzygium aromaticum  
 Thyroid gland, neoplasm  
 Zingiber officinale  
 Natural products, pharmaceutical
- RL: BIOL (Biological study); USES (Uses)  
 (composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer  
 )
- IT Alcohols, biological studies

Carbohydrates, biological studies

Corrinoids

Glycols, biological studies

Hydroquinones

Interferons

Lipids, biological studies

Polyketides

Proteins

Quassinoids

Steroids, biological studies

Ubiquinones

Waxes

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer )

IT Drug delivery systems

(emollients; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Drug delivery systems

(emulsions; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Uterus, neoplasm

(endometrium; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Drug delivery systems

(enemas; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Eucalyptus

Juglans nigra

Salvia

(extract of; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Drug delivery systems

(foams; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Drug delivery systems

(gels; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Drug delivery systems

(granules; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT Neoplasm

(head and neck; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

- IT Brain, neoplasm  
(hypothalamus; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Drug delivery systems  
(injections; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Drug delivery systems  
(liposomes; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Drug delivery systems  
(liqs., dispersions; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Drug delivery systems  
(liqs.; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Respiration, animal  
(mitochondrial; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Perfumes  
(myrrh; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Astrocyte  
(neoplasm, astrocytoma; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Drug delivery systems  
(oral; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Drug delivery systems  
(pastes; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Phenols, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polyphenols, nonpolymeric; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

- IT Drug delivery systems  
(powders; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Ubiquinones  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(reduced; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT AIDS (disease)  
(related cancer; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Lactones  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(simalikalactone; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Body, anatomical  
(sinus, tumor; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Drug delivery systems  
(solids; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Drug delivery systems  
(solns.; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Drug delivery systems  
(suppositories; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Drug delivery systems  
(suspensions; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Drug delivery systems  
(syrups; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Drug delivery systems  
(tablets; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)
- IT Connective tissue, disease  
(tumor; composition comprising mixture of ubiquinones, lactic acid

dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT 94219-29-1, CoA ligase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(acetate, inhibition of; composition comprising mixture of ubiquinones,

lactic

acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT 9001-16-5, Cytochrome c oxidase 9001-60-9, Lactic acid dehydrogenase  
9027-03-6, Ubiquinol:cytochrome c oxidoreductase 9028-04-0,  
NADH:ubiquinone oxidoreductase 9028-11-9 37205-63-3, ATP synthase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer )

IT 50-18-0, Cyclophosphamide 50-28-2, Estradiol, biological studies  
50-44-2, Mercaptopurine 50-76-0, Actinomycin D 50-81-7, Ascorbic acid, biological studies 50-91-9, Floxuridine 51-21-8, Fluorouracil  
51-75-2, Mechlorethamine 52-24-4, Thiotepa 53-19-0, Mitotane  
55-98-1, Busulfan 56-81-5, Glycerol, biological studies 57-22-7,  
Vincristine 58-85-5, Biotin 59-05-2, Methotrexate 59-30-3, Folic Acid, biological studies 59-43-8, Thiamin, biological studies 59-67-6, Niacin, biological studies 60-18-4, Tyrosine, biological studies  
63-91-2, Phenylalanine, biological studies 65-23-6, Pyridoxine  
68-19-9, Vitamin B12 77-92-9, Citric acid, biological studies 79-83-4  
83-88-5, Riboflavin, biological studies 99-96-7, biological studies  
99-96-7D, p-Hydroxybenzoic acid, polyprenol esters 117-39-5, Quercetin  
125-84-8, Aminogluthethimide 127-07-1, Hydroxyurea 146-14-5, Flavin adenine dinucleotide 146-17-8, Flavin mononucleotide 147-94-4,  
Cytarabine 148-82-3, Melphalan 154-42-7, Thioguanine 154-93-8,  
Carmustine 156-39-8 299-75-2, Treosulfan 305-03-3, Chlorambucil  
306-23-0 480-16-0, Morin 488-81-3, Ribitol 582-60-5,  
5,6-Dimethylbenzimidazole 645-05-6, Hexamethylmelamine 671-16-9,  
Procarbazine 865-21-4, Vinblastine 989-51-5, Epigallocatechin gallate  
1404-00-8, Mitomycin 1990-01-8, Glaucarubolone 2382-48-1, Ubichromenol  
2535-20-8 2920-99-2 3778-73-2, Ifosfamide 4342-03-4, Dacarbazine  
6703-77-1, Ubichromanol 7400-08-0 7439-95-4, Magnesium, biological studies  
8059-24-3, Vitamin B6 9005-25-8, Starch, biological studies  
9015-68-3, Asparaginase 10540-29-1, Tamoxifen 11056-06-7,  
Bleomycin 13010-47-4, Lomustine 13311-84-7, Flutamide 13909-09-6,  
Semustine 15663-27-1, Cisplatin 17528-72-2, Tetrahydrobiopterin  
18378-89-7, Plicamycin 18883-66-4, Streptozocin 20830-81-3,  
Daunorubicin 21679-14-1, Fludarabine 23214-92-8, Doxorubicin  
25316-40-9, Adriamycin 29767-20-2, Teniposide 33069-62-4, Taxol  
33419-42-0, Etoposide 41575-94-4, Carboplatin 53643-48-4, Vin-desine  
53714-56-0, Leuprolide 53910-25-1, Pentostatin 56420-45-2, Epirubicin  
57828-26-9, Lipoic acid 58957-92-9, Idarubicin 61825-94-3,  
Oxaliplatin 65271-80-9, Mitozantrone 71486-22-1, Vinorelbine  
71491-01-5 95058-81-4, Gemcitabine 97682-44-5, Irinotecan  
112887-68-0, Tomu-dex 114977-28-5, Taxotere 123123-32-0, Bullata-cin  
123948-87-8, Topotecan

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer )

IT 9055-15-6, Oxidoreductase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (ferredoxin, inhibition of; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT 9001-52-9, Fructose 1,6-bisphosphatase 9012-83-3, Citrate lyase  
 9013-48-3, Malate synthase 9014-19-1, Pyruvate carboxylase 9023-93-2,  
 Acetyl CoA carboxylase 9024-25-3, Aconitase 9025-76-7,  
 Phosphoglycolate phosphatase 9027-23-0, Ribulose-1,5-bisphosphate  
 carboxylase 9028-71-1, Glycolate oxidase 9045-78-7, Isocitrate lyase  
 9074-02-6, Malic enzyme 37211-69-1, 2,3-Diphosphoglycerate mutase  
 37250-89-8, Glycolaldehyde dehydrogenase 37289-44-4, Propionyl CoA  
 carboxylase 37341-55-2, Phosphoenolpyruvate carboxylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibition of; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

IT 605-94-7, 2,3-Dimethoxy-5-methyl-1,4 benzoquinone

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of; composition comprising mixture of ubiquinones, lactic acid dehydrogenase inhibitor, compound capable of augmenting oxidative phosphorylation and compound that antagonize gluconeogenesis for treatment of cancer)

L75 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:416953 HCAPLUS Full-text

DOCUMENT NUMBER: 147:62980

TITLE: Supportive care in the management of colon cancer

AUTHOR(S): Morse, Michael A.

CORPORATE SOURCE: Department of Medicine, Duke University Medical Center, Durham, NC, USA

SOURCE: Supportive Cancer Therapy (2006), 3(3), 158-170  
 CODEN: SCTUBU; ISSN: 1543-2912

PUBLISHER: CIG Media Group

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

ED Entered STN: 16 Apr 2007

AB A review. Patients with colorectal cancer present a number of supportive care challenges including those related to the underlying disease, such as gastrointestinal obstruction, nausea, anorexia, and fatigue, and those caused by the treatments, such as oral mucositis, neuropathy, and chemotherapy-induced diarrhea. Unique toxicities can accompany specific routes of administration of colon cancer drugs such as hand-foot syndrome with oral capecitabine and continuous infusion fluorouracil and biliary sclerosis with intrahepatic arterial floxuridine. The newer targeted therapies also present new toxicities, such as cardiovascular events and wound-healing complications with bevacizumab and rash and hypomagnesemia with cetuximab. Recent addns. to the therapeutic armamentarium have presented new challenges, such as oxaliplatin-induced peripheral neuropathy, capecitabine-induced hand-foot syndrome, cetuximab-induced rash, and bevacizumab-associated arterial thrombotic events, bowel perforation, hypertension, and wound-healing complications. This article focuses on the prevention and management of several of these more common symptoms and toxicities.

CC 1-0 (Pharmacology)

ST review colon cancer supportive care nausea gastrointestinal obstruction anorexia

IT Intestine, neoplasm

- (colon; well-defined care pathways have been established as supportive care in management of colon cancer patient)
- IT Nerve, disease  
(neuropathy; well-defined care pathways have been established as supportive care for management of treatment-induced neuropathy in colon cancer patient)
- IT Skin, disease  
(rash; well-defined care pathways have been established as supportive care in management of cetuximab-induced rash in colon cancer patient)
- IT Inflammation  
Mouth, disease  
(stomatitis; well-defined care pathways have been established as supportive care for management of treatment-induced oral mucositis in colon cancer patient)
- IT Anorexia  
(well-defined care pathways have been established as supportive care for management of anorexia in colon cancer patient)
- IT Fatigue, biological  
(well-defined care pathways have been established as supportive care for management of fatigue in colon cancer patient)
- IT Nausea  
(well-defined care pathways have been established as supportive care for management of nausea in colon cancer patient)
- IT Diarrhea  
(well-defined care pathways have been established as supportive care for management of treatment-induced diarrhea in colon cancer patient)
- IT Cardiovascular system, disease  
(well-defined care pathways have been established as supportive care in management of bevacizumab-induced cardiovascular disease in colon cancer patient)
- IT Wound healing  
(well-defined care pathways have been established as supportive care in management of bevacizumab-induced wound-healing complication in colon cancer patient)
- IT Human  
(well-defined care pathways have been established as supportive care in management of colon cancer patient)
- IT 7439-95-4, Magnesium, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(hypomagnesemia; well-defined care pathways have been established as supportive care in management of cetuximab-induced hypomagnesemia in colon cancer patient)
- IT 50-91-9, Floxuridine  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(intrahepatic arterial floxuridine accompanied biliary sclerosis in colon cancer patient)
- IT 51-21-8, Fluorouracil  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(oral capecitabine and continuous of fluorouracil accompanied hand-foot syndrome in colon cancer)
- IT 154361-50-9, Capecitabine  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(oral capecitabine and continuous of fluorouracil accompanied hand-foot syndrome in colon cancer patient)
- IT 216974-75-3, Bevacizumab



10/501318

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(well-defined care pathways have been established as supportive care in  
management of bevacizumab-induced cardiovascular disease and  
wound-healing complication in colon cancer patient)

IT 205923-56-4, Cetuximab

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(well-defined care pathways have been established as supportive care in  
management of cetuximab-induced rash and hypomagnesemia in colon  
cancer patient)

IT 61825-94-3, Oxaliplatin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(well-defined care pathways have been established as supportive care in  
management of oxaliplatin-induced peripheral neuropathy in  
colon cancer patient)

REFERENCE COUNT: 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L75 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:534192 HCAPLUS Full-text

DOCUMENT NUMBER: 141:89101

TITLE: Preparation of carboxylic acid, phosphate, or  
phosphonate substituted (quinazolin-4-yl)amines as  
capsaicin receptor modulators

INVENTOR(S): Bakthavatchalam, Rajagopal; Blum, Charles A.;  
Briellmann, Harry; Caldwell, Timothy M.; De Lombaert,  
Stephane; Hodgetts, Kevin J.; Zheng, Xiaozhang

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: PCT Int. Appl., 113 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004055004	A1	20040701	WO 2003-US39607	20031212 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2509239	A1	20040701	CA 2003-2509239	20031212 <--
AU 2003300898	A1	20040709	AU 2003-300898	20031212 <--
US 2004156869	A1	20040812	US 2003-735607	20031212 <--
EP 1569926	A1	20050907	EP 2003-813411	20031212 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1726205	A	20060125	CN 2003-80105815	20031212 <--
JP 2006515847	T	20060608	JP 2004-560828	20031212 <--
US 2006089354	A1	20060427	US 2005-539031	20050613 <--

PRIORITY APPLN. INFO.:

US 2002-433139P

P 20021213 &lt;--

WO 2003-US39607

W 20031212 &lt;--

OTHER SOURCE(S): MARPAT 141:89101

ED Entered STN: 02 Jul 2004

AB Title acid-substituted (quinazolin-4-yl)amines and analogs (I) [wherein V, W, X, Y, and Z = independently N, CR1, with the proviso that at least one of V and X = N; U = N, CR2, with the proviso that if V and X = N, then U = CR2; R1 = independently H, halo, OH, CN, NH2, CO2H, (halo)alkyl, (halo)alkoxy, alkoxy carbonyl, (di)alkylamino; R2 = H, halo, CN, NO2, (un)substituted alkyl, alkenyl, or alkynyl optionally interrupted by O, S, SO, SO2, CO, OCO, CO2, OCO2, CHNH, NHCO, NHSO2, SO2NH, NH, OPO2(OH), or PO2(OH); Ar1 and Ar2 = independently (un)substituted carbocyclyl, heterocyclyl; and pharmaceutically acceptable forms thereof] were prepared as modulators of capsaicin receptors, especially the vanilloid receptor 1 (VR1). For example, 2-tert-butyl-5-nitrophenol was condensed with 2-(tert-butyldimethylsilyloxy)ethanol, and the resulting nitrophenyl ether reduced to give the substituted aniline. Condensation of the phenylamine with 4-chloro-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-ol, followed by deprotection, coupling with L-proline Me ester, and saponification provided II. In competition binding assays, invention compds. exhibited  $K_i \leq 1 \mu\text{M}$  for VR1 expressed in human embryonic kidney (HEK293) cells. Thus, I and their pharmaceutical compns. are useful for treating disorders associated with pathol. receptor activation, such as pain, in humans, domesticated companion animals, and livestock animals (no data).

IC ICM C07D401-04

ICS C07D471-04; C07F009-09; C07F009-38

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

IT Drug delivery systems

(injections; preparation of acid-substituted (quinazolin-4-yl)amines as VR1 inhibitors for treatment of pain and other VR1-mediated conditions)

IT Drug delivery systems

(oral; preparation of acid-substituted (quinazolin-4-yl)amines as VR1 inhibitors for treatment of pain and other VR1-mediated conditions)

IT Dyspepsia

Flatulence

Headache

Menstruation

Musculoskeletal diseases

Neoplasm

Osteoarthritis

Parturition

Rheumatoid arthritis

Surgery

(treatment of pain associated with; preparation of acid-substituted (quinazolin-4-yl)amines as VR1 inhibitors for treatment of pain and other VR1-mediated conditions)

IT 95-92-1, Diethyl oxalate 455-14-1, 4-Trifluoromethylaniline

769-92-6, 4-tert-Butylaniline 1623-08-1, Dibenzyl phosphate 2577-48-2,

L-Proline methyl ester 6066-82-6, N-Hydroxysuccinimide 66762-68-3

102229-10-7, 2-(tert-Butyldimethylsilyloxy)ethanol 442847-11-2,

2-tert-Butyl-5-nitrophenol 573675-83-9, 4-Chloro-7-(3-

trifluoromethylpyridin-2-yl)quinazoline 714956-69-1 714956-71-5

714956-74-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of acid-substituted (quinazolin-4-yl)amines as VR1 inhibitors for treatment of pain and other VR1-mediated conditions)

IT 7440-70-2, Calcium, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

10/501318

(reducing capsaicin receptor mobilization of; preparation of  
acid-substituted (quinazolin-4-yl)amines as VR1 inhibitors for  
treatment of pain and other VR1-mediated conditions)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:41116 HCAPLUS Full-text

DOCUMENT NUMBER: 140:105248

TITLE: Synthesis and antiproliferative effects of  
1 $\alpha$ ,24(S)-dihydroxyvitamin D<sub>2</sub>, and use with other  
agents

INVENTOR(S): Bishop, Charles W.; Knutson, Joyce C.; Strugnelli,  
Stephen; Mazess, Richard B.

PATENT ASSIGNEE(S): Bone Care International, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S.  
Pat. Appl. 2002 32,179.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004009958	A1	20040115	US 2003-390953	20030318 <--
WO 9212165	A1	19920723	WO 1992-US313	19920107 <--
W: AU, BR, CA, FI, HU, JP, KP, KR, NO, PL, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
EP 914825	A2	19990512	EP 1998-110802	19920107 <--
EP 914825	A3	19990519		
EP 914825	B1	20030521		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC				
US 5786348	A	19980728	US 1995-477930	19950607 <--
US 5789397	A	19980804	US 1995-485184	19950607 <--
US 6166000	A	20001226	US 1995-472499	19950607 <--
US 6143910	A	20001107	US 1998-211984	19981214 <--
US 6251883	B1	20010626	US 1998-211991	19981214 <--
US 2002032179	A1	20020314	US 2001-891963	20010626 <--
US 6538037	B2	20030325		
CA 2451039	A1	20030109	CA 2002-2451039	20020626 <--
WO 2003002110	A1	20030109	WO 2002-US20317	20020626 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
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AU 2002315463	A1	20030303	AU 2002-315463	20020626 <--
AU 2002315463	B2	20070531		
EP 1408939	A1	20040421	EP 2002-742318	20020626 <--
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CN 1520288	A	20040811	CN 2002-812836	20020626 <--
JP 2004535441	T	20041125	JP 2003-508349	20020626 <--
AU 2004222310	A1	20040930	AU 2004-222310	20040316 <--
CA 2517125	A1	20040930	CA 2004-2517125	20040316 <--

10/501318

WO 2004082631 A2 20040930 WO 2004-US8136 20040316 <--  
 WO 2004082631 A3 20051229  
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,  
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 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
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 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,  
 SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,  
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 EP 1617810 A2 20060125 EP 2004-749390 20040316 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK  
 BR 2004008468 A 20060404 BR 2004-8468 20040316 <--  
 CN 1774242 A 20060517 CN 2004-80007470 20040316 <--  
 JP 2006520791 T 20060914 JP 2006-507271 20040316 <--

PRIORITY APPLN. INFO.:

US 1991-637867 B2 19910108 <--  
 WO 1992-US313 A2 19920107 <--  
 US 1992-940246 B1 19920828 <--  
 US 1994-275641 B1 19940714 <--  
 US 1995-515801 B2 19950816 <--  
 US 1998-211991 A2 19981214 <--  
 US 2001-891963 A2 20010626 <--  
 EP 1992-904947 A3 19920107 <--  
 WO 2002-US20317 W 20020626 <--  
 US 2003-390953 A 20030318 <--  
 WO 2004-US8136 A 20040316

ED Entered STN: 18 Jan 2004

AB The invention discloses the hormonally active, natural metabolite 1 $\alpha$ ,24(S)-  
 dihydroxyvitamin D2 and a method of preparing this metabolite and the nonbiol.  
 epimer 1 $\alpha$ ,24(R)-dihydroxyvitamin D2. The invention also relates to a  
 pharmaceutical composition including a pharmaceutically effective amount of  
 1 $\alpha$ ,24(S)-dihydroxyvitamin D2, to a method of controlling abnormal calcium  
 metabolism by administering a pharmaceutically effective amount of the  
 compound, and to a method of treating hyperproliferative diseases by  
 administering the compound. The method also includes the co-administration of  
 cytotoxic agents with the 1 $\alpha$ ,24(S)-dihydroxyvitamin D2.

IC ICM A61K031-7072

ICS A61K031-704; A61K031-59; A61K031-525; A61K031-337; A61K031-28

INCL 514167000; X51-4 5.0; X51-425.1; X51-4 3.4; X51-444.9; X51-449.2

CC 1-6 (Pharmacology)

Section cross-reference(s): 32, 63

IT Prostate gland, neoplasm

(adenocarcinoma; synthesis and antiproliferative effects of

1 $\alpha$ ,24(S)-dihydroxyvitamin D2, and use with other agents)

IT Drug delivery systems

(injections, i.v.; synthesis and antiproliferative effects of

1 $\alpha$ ,24(S)-dihydroxyvitamin D2, and use with other agents)

IT Drug delivery systems

(injections; synthesis and antiproliferative effects of

1 $\alpha$ ,24(S)-dihydroxyvitamin D2, and use with other agents)

IT Drug delivery systems

(oral; synthesis and antiproliferative effects of

1 $\alpha$ ,24(S)-dihydroxyvitamin D2, and use with other agents)

IT Acute lymphocytic leukemia

Acute myeloid leukemia

Alkylating agents, biological  
 Angiogenesis inhibitors  
 Antitumor agents  
 Chronic lymphocytic leukemia  
 Chronic myeloid leukemia  
 Cosmetics  
 Drug interactions  
 Human  
 Mammary gland, neoplasm  
 Myelodysplastic syndromes  
 Osteoporosis  
 Vaccines

(synthesis and antiproliferative effects of  $1\alpha,24(S)$ -  
 dihydroxyvitamin D<sub>2</sub>, and use with other agents)

IT 50-14-6, Vitamin D<sub>2</sub> 50-18-0, Cyclophosphamide 50-35-1, Thalidomide  
 51-21-8, 5-Fluoro-uracil 53-03-2, Prednisone 57-22-7, Vincristine  
 59-05-2, Methotrexate 127-07-1, Hydroxyurea 148-82-3, Melphalan  
 154-93-8 302-79-4, Retinoic acid 865-21-4, Vinblastine 1404-00-8,  
 Mitomycin 4891-15-0, Estramustine phosphate 7440-06-4D, Platinum,  
 compds. 7689-03-4, Camptothecin 15663-27-1, Cisplatin 20830-81-3,  
 Daunomycin 21679-14-1, Fludarabine 23214-92-8, Doxorubicin  
 25316-40-9, Adriamycin 29069-24-7, Prednimustine 33069-62-4,  
 Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin 58957-92-9,  
 Idarubicin 60133-18-8 61825-94-3, Oxaliplatin  
 62683-29-8, Colony stimulating factor 110172-45-7, CI-973 114977-28-5,  
 Docetaxel 129580-63-8, JM-216 174722-31-7, Rituximab 180288-69-1,  
 Trastuzumab

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(synthesis and antiproliferative effects of  $1\alpha,24(S)$ -  
 dihydroxyvitamin D<sub>2</sub>, and use with other agents)

IT 7440-70-2, Calcium, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (transport; synthesis and antiproliferative effects of  
 $1\alpha,24(S)$ -dihydroxyvitamin D<sub>2</sub>, and use with other agents)

L75 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:176560 HCAPLUS Full-text

DOCUMENT NUMBER: 140:217656

TITLE: Preparation of aryl-substituted tetrahydropyrimidines  
 and related compounds as melanocortin-4 receptor  
 binding compounds

INVENTOR(S): Maguire, Martin P.; Dai, Mingshi; Vos, Tricia J.

PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA

SOURCE: U.S., 216 pp., Cont.-in-part of U.S. Ser. No. 632309.  
 CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6699873	B1	20040302	US 2001-778468	20010207 <--
WO 2002062766	A2	20020815	WO 2002-US3566	20020207 <--
WO 2002062766	A3	20021003		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,			
	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,			
	GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,			

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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002250029 A1 20020819 AU 2002-250029 20020207 <--  
EP 1363890 A2 20031126 EP 2002-718920 20020207 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2004082779 A1 20040429 US 2003-462436 20030616 <--

PRIORITY APPLN. INFO.: US 1999-147288P P 19990804 <--  
US 2000-223277P P 20000803 <--  
US 2000-632309 A2 20000804 <--  
US 2001-778468 A 20010207 <--  
WO 2002-US3566 W 20020207 <--

OTHER SOURCE(S): MARPAT 140:217656

ED Entered STN: 04 Mar 2004

AB The title compds. [I and related compds.; A = CH, CF, CCl, C(alkyl), etc.; B = CH, CF, CCl, C(alkyl), etc.; C = CH, CCl, S, etc.; G, H = CH<sub>2</sub>, S; D = CH<sub>2</sub>; E, F = (un)substituted CH<sub>2</sub>; X = C(alkoxy); Y = CH, C(C.tplbond.CH), CCl, CBr, CCl, CF; Z = CH; or pharmaceutically acceptable salts thereof] were prepared for treating a melanocortin-4 receptor (MC4-R) associated state in a mammal. For example, stirring a solution of  $\alpha$ -tolunitrile with diisopropylamine and BuLi in hexanes at -78° under nitrogen for 1 h, followed by addition of HMPA and 1-chloromethylnaphthalene in THF, afforded 2-(2-naphthalen-1-ylethyl)benzonitrile. Heating the benzonitrile with 1,3-diaminopropane in the presence of H<sub>2</sub>S at 80° for 72 h gave the tetrahydropyrimidinyl cycloaddn. product II. The latter exhibited exemplary inhibition of MC4-R in a scintillation proximity assay. I are useful for the treatment of disorders associated with pigmentation, bones, or weight loss (no data).

IC ICM C07D235-06

ICS C07D239-06; C07D233-20; A61K031-4184; A61K031-505

INCL 514256000; 544242000; 544335000

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

IT Cachexia

(cancerous; preparation of aryl-substituted tetrahydropyrimidines and related compds. as melanocortin-4 receptor binding compds. for treatment of pigmentation, bone, and weight loss disorders)

IT Drug delivery systems

(oral; preparation of aryl-substituted tetrahydropyrimidines and related compds. as melanocortin-4 receptor binding compds. for treatment of pigmentation, bone, and weight loss disorders)

IT 59-98-3P 110-85-0P, Piperazine, preparation 130-61-0P 550-99-2P

936-49-2P 1150-41-0P 1670-14-0P 3552-64-5P 4205-91-8P 5361-15-9P

20980-22-7P 22232-71-9P 22746-09-4P 34803-66-2P 50693-78-2P

50736-94-2P 53761-49-2P 54050-86-1P 56406-50-9P 62838-27-1P

79458-26-7P 87394-63-6P 91066-99-8P 97603-94-6P 99931-82-5P

106824-02-6P 132834-58-3P 146797-21-9P 151965-25-2P 155204-26-5P,

4-Fluoro-N-[2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl]-N-pyridin-2-

ylbenzamide 175203-79-9P 179756-91-3P 292870-46-3P 314240-83-0P,

2-(2-Bromo-phenyl)-4,5-dihydro-1H-imidazole hydrochloride 325798-38-7P,

2-[2-(4-Benzoyloxybenzylsulfanyl)phenyl]-1,4,5,6-tetrahydropyrimidine

325800-01-9P, 2-(2-Benzylsulfanylphenyl)-1,4,5,6-tetrahydropyrimidine

325800-58-6P, 2-[2-(2-Methylnaphthalen-1-ylmethylsulfanyl)phenyl]-1,4,5,6-

tetrahydropyrimidine 325800-59-7P, 1-[2-[2-(2-Chloro-6-

fluorobenzylsulfanyl)phenyl]-5,6-dihydro-4H-pyrimidin-1-yl]ethanone

325801-15-8P, 2-[2-(Naphthalen-1-yloxymethyl)phenyl]-1,4,5,6-

tetrahydropyrimidine 325801-17-0P, 2-[2-(5-Bromo-2-

methoxybenzylsulfanyl)phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole  
 325801-23-8P, 2-[4-Bromo-2-(5-bromo-2-methoxybenzylsulfanyl)phenyl]-  
 1,4,5,6-tetrahydropyrimidine 325801-24-9P, 2-[2-(5-Bromo-2-  
 methoxybenzylsulfanyl)-5-methylphenyl]-1,4,5,6-tetrahydropyrimidine  
 325801-27-2P, 2-[2-(5-Chloro-2-methoxybenzylsulfanyl)phenyl]-1,4,5,6-  
 tetrahydropyrimidine 325801-33-0P, 2-[2-(5-Bromo-2-  
 methoxybenzylsulfanyl)-5-fluorophenyl]-1,4,5,6-tetrahydropyrimidine  
 325801-35-2P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3-fluorophenyl]-  
 1,4,5,6-tetrahydropyrimidine 325823-81-2P, 1-[2-[2-(5-Bromo-2-  
 methoxybenzylsulfanyl)phenyl]-5,6-dihydro-4H-pyrimidin-1-yl]-3-methylbutan-  
 1-one 325823-82-3P, 1-[2-[2-(5-Bromo-2-methoxybenzylsulfanyl)phenyl]-5,6-  
 dihydro-4H-pyrimidin-1-yl]-2-phenylethanone 325823-83-4P,  
 2-[3-(5-Bromo-2-methoxybenzylsulfanyl)pyridin-2-yl]-1,4,5,6-  
 tetrahydropyrimidine 325823-84-5P, N-[2-(5-Bromo-2-  
 methoxybenzylsulfanyl)phenyl]guanidine 325823-88-9P,  
 (5-Bromo-2-methoxybenzyl)[2-(1,4,5,6-tetrahydropyrimidin-2-yl)phenyl]amine  
 325823-92-5P, 2-[3-(5-Bromo-2-methoxybenzylsulfanyl)pyrazin-2-yl]-1,4,5,6-  
 tetrahydropyrimidine 325823-96-9P, 2-[3-Chloro-2-(2-methoxynaphthalen-1-  
 ylsulfanylmethyl)phenyl]-1,4,5,6-tetrahydropyrimidine 325824-00-8P,  
 2-[1-(2-Naphthalen-1-ylethyl)-1H-pyrrol-2-yl]-1,4,5,6-tetrahydropyrimidine  
 325826-71-9P, 4-tert-Butyl-N-naphthalen-1-ylmethyl-N-(2-piperidin-1-  
 ylethyl)benzamide 325826-87-7P, N,N-Dimethyl-N'-naphthalen-2-ylmethyl-N'-  
 naphthalen-1-ylmethylpropane-1,3-diamine 325826-98-0P,  
 N-(5-Bromo-2-methoxybenzyl)-N',N'-dimethyl-N-naphthalen-1-ylmethylpropane-  
 1,3-diamine 325827-19-8P, 3-[2-(5-Bromo-2-methoxybenzylsulfanyl)benzylam-  
 ino]propan-1-ol 325827-20-1P, 3-[2-(5-Bromo-2-  
 methoxybenzylsulfanyl)benzylamino]-3-methylbutan-1-ol 325827-28-9P,  
 1-[2-(5-Bromo-2-methoxybenzylsulfanyl)benzyl]pyrrolidin-3-ol  
 325828-03-3P 325828-05-5P, 1-(2-Naphthalen-1-ylethyl)piperidine-2-  
 carboxylic acid methyl ester 325828-18-0P 325828-24-8P 325828-26-0P,  
 [2-(Naphthalen-1-ylmethylsulfanyl)phenyl]carbamic acid  
 2-dimethylaminoethyl ester 325828-53-3P, 1-Phenyl-3-piperazin-1-yl-  
 5,6,7,8-tetrahydroisoquinoline-4-carbonitrile 325828-56-6P,  
 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)phenyl]-6-ethyl-1,4,5,6-  
 tetrahydropyrimidine 325828-61-3P, 2-[2-(2,5-  
 Dimethoxyphenylsulfanylmethyl)phenyl]-1,4,5,6-tetrahydropyrimidine  
 325828-72-6P, 2-[2-[2-(5-Bromo-2-methoxyphenyl)ethyl]phenyl]-1,4,5,6-  
 tetrahydropyrimidine 325828-80-6P, 2-[2-(2-Methoxy-5-  
 trifluoromethylbenzylsulfanyl)phenyl]-1,4,5,6-tetrahydropyrimidine  
 325828-97-5P, 2-[2-[2-(5-Bromo-2-methoxyphenyl)ethyl]-3-  
 trifluoromethylphenyl]-1,4,5,6-tetrahydropyrimidine 325829-05-8P,  
 5,5-Dimethyl-2-[2-(2-naphthalen-1-ylethyl)phenyl]-4,5-dihydro-1H-imidazole  
 325829-06-9P, 2-[3-Fluoro-2-(2-naphthalen-1-ylethyl)phenyl]-5,5-dimethyl-  
 4,5-dihydro-1H-imidazole 325829-07-0P, 2-[2-(5-Bromo-2-  
 methoxybenzylsulfanyl)-3,5-difluorophenyl]-1,4,5,6-tetrahydropyrimidine  
 325829-08-1P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3,5-difluorophenyl]-  
 5,5-dimethyl-4,5-dihydro-1H-imidazole 325829-09-2P, 3-(2-Naphthalen-1-  
 ylethyl)-2-(1,4,5,6-tetrahydropyrimidin-2-yl)phenylamine 325829-10-5P  
 325829-11-6P, 1-[2-(2-Naphthalen-1-ylethyl)phenyl]ethane-1,2-diamine  
 325829-12-7P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)phenyl]-4-methyl-4,5-  
 dihydro-1H-imidazole 325829-13-8P, 2-[2-(5-Bromo-2-  
 methoxybenzylsulfanyl)-3-fluorophenyl]-4-methyl-4,5-dihydro-1H-imidazole  
 325829-14-9P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3-chlorophenyl]-4-  
 methyl-4,5-dihydro-1H-imidazole 325829-40-1P, 2-[3-Fluoro-2-(naphthalen-  
 1-ylsulfanylmethyl)phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole  
 325829-54-7P, 2-[2-[2-(5-Bromo-2-methoxyphenyl)-1-methylethyl]phenyl]-  
 1,4,5,6-tetrahydropyrimidine 325829-68-3P, 2-[2-(5-Bromo-2-  
 methoxybenzylsulfanyl)-3-fluoro-4-trifluoromethylphenyl]-4,4-dimethyl-4,5-  
 dihydro-1H-imidazole 325829-70-7P, 2-[2-(5-Bromo-2-  
 methoxybenzylsulfanyl)-3-fluoro-4-trifluoromethylphenyl]-5,5-dimethyl-

1,4,5,6-tetrahydropyrimidine 325829-71-8P, 2-[3-Methoxy-2-(2-naphthalen-1-ylethyl)phenyl]-1,4,5,6-tetrahydropyrimidine 325829-76-3P,  
 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3-chlorophenyl]-1,4,5,6-tetrahydropyrimidin-5-ol 325829-77-4P, 2-[2-(2-(5-Bromo-2-methoxyphenyl)ethyl)-3-methoxyphenyl]-1,4,5,6-tetrahydropyrimidine 325959-09-9P, 2-[2-(2-Chloro-6-fluorobenzylsulfanyl)phenyl]-1,4,5,6-tetrahydropyrimidine hydrochloride 325959-37-3P 325959-77-1P,  
 2-[2-(5-Bromo-2-methoxyphenylsulfanylmethyl)phenyl]-1,4,5,6-tetrahydropyrimidine hydrochloride 325959-78-2P 325959-80-6P  
 325959-81-7P 325959-82-8P 325959-83-9P 325959-84-0P 326480-55-1P  
 326480-56-2P 326480-57-3P 326480-58-4P 326480-59-5P 326480-60-8P  
 326480-61-9P 326480-62-0P 326480-63-1P 326480-64-2P 326480-65-3P  
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 326480-71-1P 326480-72-2P 326480-73-3P 326480-74-4P 326480-75-5P  
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 326480-98-2P 326480-99-3P 326481-00-9P 326481-01-0P,  
 4-Phenyl-2-piperazin-1-yl-6-p-tolyl-pyrimidine 326481-02-1P,  
 N-Benzyl-N-(3-chloro-benzyl)-N',N'-dimethylethane-1,2-diamine  
 326481-03-2P, N-Benzyl-N-(4-bromo-benzyl)-N',N'-dimethylethane-1,2-diamine  
 326481-04-3P, N-Benzyl-N-(3,4-dichloro-benzyl)-N',N'-dimethylethane-1,2-diamine  
 326481-05-4P, 7-Chloro-4,8-dimethyl-2-piperazin-1-yl-quinoline  
 326481-06-5P, 7-Chloro-4,8-dimethyl-2-piperazin-1-yl-quinoline  
 oxalate 326481-07-6P, 7-Chloro-4,8-dimethyl-2-piperazin-1-yl-quinoline  
 formate 326481-08-7P, 2,7-Dichloro-4,8-dimethyl-quinoline  
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 326482-43-3P 326482-44-4P 326482-45-5P 326482-46-6P 326482-47-7P  
 326482-48-8P 326482-49-9P 326482-50-2P 326482-51-3P 326482-52-4P  
 326482-53-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(MC4-R binding compound; preparation of aryl-substituted tetrahydropyrimidines and related compds. as melanocortin-4 receptor binding compds. for treatment of pigmentation, bone, and weight loss disorders)

IT 7440-70-2, Calcium, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study) (depletion in bone; preparation of aryl-substituted tetrahydropyrimidines and related compds. as melanocortin-4 receptor binding compds. for treatment of pigmentation, bone, and weight loss disorders)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



10/501318

L75 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2003:554029 HCAPLUS Full-text  
 DOCUMENT NUMBER: 139:111695  
 TITLE: Administration of calcium and magnesium for protection  
 against the neurotoxicity of  
 oxaliplatin  
 INVENTOR(S): Gamelin, Laurence; Gamelin, Erick; Boisdron, Celle  
 Michele; Morel, Alain  
 PATENT ASSIGNEE(S): Centre Regional de Lutte Contre le Cancer d'Angers,  
 Fr.  
 SOURCE: Fr. Demande, 22 pp.  
 CODEN: FRXXBL  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2834641	A1	20030718	FR 2002-390	20020114 <--
FR 2834641	B1	20050422		
WO 2003059361	A1	20030724	WO 2003-FR98	20030114 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003216720	A1	20030730	AU 2003-216720	20030114 <--
EP 1465642	A1	20041013	EP 2003-712239	20030114 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005519062	T	20050630	JP 2003-559523	20030114 <--
US 2005148661	A1	20050707	US 2005-501318	20050225 <--
PRIORITY APPLN. INFO.:			FR 2002-390	A 20020114 <--
			WO 2003-FR98	W 20030114 <--

ED Entered STN: 20 Jul 2003  
 AB The invention discloses products including calcium, injectable magnesium and  
 an injectable product which releases oxalate during its metabolism, as a  
 useful combination for administration simultaneously, sequentially or sep. in  
 anticancer and antiviral therapy.  
 IC ICM A61K033-06  
 ICS A61P035-00; A61P031-12; A61K031-282  
 CC 1-11 (Pharmacology)  
 Section cross-reference(s): 63  
 ST calcium magnesium oxaliplatin neurotoxicity  
 protection; antiviral antitumor therapy oxaliplatin  
 calcium magnesium neuroprotection  
 IT Antitumor agents  
 Antiviral agents  
 Drug metabolism  
 Human  
 Neoplasm  
 Nerve  
 Neurotoxicity  
 (calcium and magnesium for protection against oxaliplatin)

neurotoxicity)

IT Platelet (blood)  
(disease, thrombocytopenia; calcium and magnesium for protection against oxaliplatin neurotoxicity)

IT Drug delivery systems  
(injections; calcium and magnesium for protection against oxaliplatin neurotoxicity)

IT Nerve, disease  
Nerve, disease  
(neuropathy; calcium and magnesium for protection against oxaliplatin neurotoxicity)

IT Cytoprotective agents  
Nervous system agents  
(neuroprotective agents; calcium and magnesium for protection against oxaliplatin neurotoxicity)

IT Agranulocytosis  
(neutropenia; calcium and magnesium for protection against oxaliplatin neurotoxicity)

IT Drug delivery systems  
(oral; calcium and magnesium for protection against oxaliplatin neurotoxicity)

IT Tooth, disease  
(paresthesia; calcium and magnesium for protection against oxaliplatin neurotoxicity)

IT Blood, disease  
(thrombocytopenia; calcium and magnesium for protection against oxaliplatin neurotoxicity)

IT Infection  
(viral; calcium and magnesium for protection against oxaliplatin neurotoxicity)

IT 61825-94-3, Oxaliplatin  
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(calcium and magnesium for protection against oxaliplatin neurotoxicity)

IT 299-28-5, Calcium gluconate 471-34-1  
, Calcium carbonate, biological studies 7439-95-4; Magnesium, biological studies 7440-70-2, Calcium, biological studies 7487-88-9, Magnesium sulfate, biological studies 10043-52-4, Calcium chloride, biological studies 11116-97-5, Calcium gluconolactate 33659-28-8 135701-98-3, Magnesium pidolate  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(calcium and magnesium for protection against oxaliplatin neurotoxicity)

IT 144-62-7, Oxalic acid, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(oxalate metabolic release; calcium and magnesium for protection against oxaliplatin neurotoxicity)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2002:615577 HCAPLUS Full-text  
DOCUMENT NUMBER: 137:169536  
TITLE: Preparation of aryl-substituted tetrahydropyrimidines and related compounds as melanocortin-4 receptor binding compounds

10/501318

INVENTOR(S): Maguire, Martin P.; Dai, Mingshi; Vos, Tricia J.  
 PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 228 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062766	A2	20020815	WO 2002-US3566	20020207 <--
WO 2002062766	A3	20021003		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6699873	B1	20040302	US 2001-778468	20010207 <--
AU 2002250029	A1	20020819	AU 2002-250029	20020207 <--
EP 1363890	A2	20031126	EP 2002-718920	20020207 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:  
 US 2001-778468 A 20010207 <--  
 US 1999-147288P P 19990804 <--  
 US 2000-223277P P 20000803 <--  
 US 2000-632309 A2 20000804 <--  
 WO 2002-US3566 W 20020207 <--

OTHER SOURCE(S): MARPAT 137:169536

ED Entered STN: 16 Aug 2002

AB Title compds. I [wherein A and B = independently (un)substituted biaryl, (hetero)aryl, Ph, (cyclo)alkyl, (cyclo)alkoxy, alkenyl, alkynyl, OH, acyl(oxy), carbamoyl, amino, thiol, amidino, imino, NO<sub>2</sub>, N<sub>3</sub>, etc.; L1 and L2 = covalent bond or (un)substituted alkyl optionally interrupted by O, S, or N; r = covalent bond, CH, CH<sub>2</sub>, CHR<sub>1</sub>, CR<sub>1</sub>R<sub>2</sub>, or H; t = CH, CH<sub>2</sub>, CHR<sub>3</sub>, CR<sub>3</sub>R<sub>4</sub>, or H; s = CHR<sub>5</sub>, CR<sub>5</sub>R<sub>6</sub>, or absent; R = H, (un)substituted alkyl, arylalkyl, or heteroalkyl, and may optionally be linked to A, B, L1, or L2; R1-R6 = independently (un)substituted alkyl, halo, thiol, thioether, thioalkyl, alkoxy, and may be optionally linked to each other to form addnl. ring moieties, e.g., quinoxalinyl; or pharmaceutically acceptable salts thereof] were prepared as melanocortin-4 receptor binding (MC4-R) compds. For example, stirring a solution of α-tolunitrile with diisopropylamine and BuLi in hexanes at -78° under nitrogen for 1 h, followed by addition of HMPA and 1-chloromethylnaphthalene in THF, afforded 2-(2-naphthalen-1-ylethyl)benzonitrile. Heating the benzonitrile with 1,3-diaminopropane in the presence of H<sub>2</sub>S at 80° for 72 h gave the tetrahydropyrimidinyl cycloaddn. product II. The latter exhibited exemplary inhibition of MC4-R in a scintillation proximity assay. I are useful for the treatment of disorders associated with pigmentation, bones, or weight loss (no data).

IC ICM C07D235-06

ICS C07D239-06; C07D233-20; A61K031-4184; A61K031-4164; A61K031-505

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT Cachexia

(cancerous; preparation of aryl-substituted tetrahydropyrimidines and related compds. as melanocortin-4 receptor binding compds. for

treatment of pigmentation, bone, and weight loss disorders)

IT Drug delivery systems

(oral; preparation of aryl-substituted tetrahydropyrimidines and related compds. as melanocortin-4 receptor binding compds. for treatment of pigmentation, bone, and weight loss disorders)

- IT 325829-01-4P, 2-[3-Fluoro-2-(2-naphthalen-1-ylethyl)phenyl]-1,4,5,6-tetrahydropyrimidine 325829-02-5P, [2-(5-Bromo-2-methoxybenzylsulfanyl)-3-chlorobenzyl][3-(2-methylpiperidin-1-yl)propyl]amine 325829-03-6P, 1-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3-chlorobenzyl]pyrrolidin-3-ylamine 325829-04-7P, 1-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3-chlorobenzyl]piperazine 325829-05-8P, 5,5-Dimethyl-2-[2-(2-naphthalen-1-ylethyl)phenyl]-4,5-dihydro-1H-imidazole 325829-06-9P, 2-[3-Fluoro-2-(2-naphthalen-1-ylethyl)phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole 325829-07-0P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3,5-difluorophenyl]-1,4,5,6-tetrahydropyrimidine 325829-08-1P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3,5-difluorophenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole 325829-09-2P, 3-(2-Naphthalen-1-ylethyl)-2-(1,4,5,6-tetrahydropyrimidin-2-yl)phenylamine 325829-10-5P 325829-11-6P, 1-[2-(2-Naphthalen-1-ylethyl)phenyl]ethane-1,2-diamine 325829-12-7P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)phenyl]-4-methyl-4,5-dihydro-1H-imidazole 325829-13-8P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3-fluorophenyl]-4-methyl-4,5-dihydro-1H-imidazole 325829-14-9P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3-chlorophenyl]-4-methyl-4,5-dihydro-1H-imidazole 325829-26-3P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3,4-difluorophenyl]-1,4,5,6-tetrahydropyrimidine 325829-40-1P, 2-[3-Fluoro-2-(naphthalen-1-ylsulfanylmethyl)phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole 325829-54-7P, 2-[2-[2-(5-Bromo-2-methoxyphenyl)-1-methylethyl]phenyl]-1,4,5,6-tetrahydropyrimidine 325829-68-3P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3-fluoro-4-trifluoromethylphenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole 325829-70-7P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3-fluoro-4-trifluoromethylphenyl]-5,5-dimethyl-1,4,5,6-tetrahydropyrimidine 325829-71-8P, 2-[3-Methoxy-2-(2-naphthalen-1-ylethyl)phenyl]-1,4,5,6-tetrahydropyrimidine 325829-76-3P, 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-3-chlorophenyl]-1,4,5,6-tetrahydropyrimidin-5-ol 325829-77-4P, 2-[2-[2-(5-Bromo-2-methoxyphenyl)ethyl]-3-methoxyphenyl]-1,4,5,6-tetrahydropyrimidine 325959-09-9P, 2-[2-(2-Chloro-6-fluorobenzylsulfanyl)phenyl]-1,4,5,6-tetrahydropyrimidine hydrochloride 325959-37-3P 325959-77-1P, 2-[2-(5-Bromo-2-methoxyphenylsulfanylmethyl)phenyl]-1,4,5,6-tetrahydropyrimidine hydrochloride 325959-78-2P 325959-80-6P 325959-81-7P 325959-82-8P 325959-83-9P 325959-84-0P 326480-55-1P 326480-56-2P 326480-57-3P 326480-58-4P 326480-59-5P 326480-60-8P 326480-61-9P 326480-62-0P 326480-63-1P 326480-64-2P 326480-65-3P 326480-66-4P 326480-67-5P 326480-68-6P 326480-69-7P 326480-70-0P 326480-71-1P 326480-72-2P 326480-73-3P 326480-74-4P 326480-75-5P 326480-76-6P 326480-77-7P 326480-78-8P 326480-79-9P 326480-81-3P 326480-82-4P 326480-83-5P 326480-84-6P 326480-85-7P 326480-86-8P 326480-88-0P 326480-89-1P 326480-90-4P 326480-91-5P 326480-92-6P 326480-93-7P 326480-94-8P 326480-95-9P 326480-96-0P 326480-97-1P 326480-98-2P 326480-99-3P 326481-00-9P 326481-01-0P, 4-Phenyl-2-piperazin-1-yl-6-p-tolyl-pyrimidine 326481-02-1P, N-Benzyl-N-(3-chloro-benzyl)-N',N'-dimethylethane-1,2-diamine 326481-03-2P, N-Benzyl-N-(4-bromo-benzyl)-N',N'-dimethylethane-1,2-diamine 326481-04-3P, N-Benzyl-N-(3,4-dichloro-benzyl)-N',N'-dimethylethane-1,2-diamine 326481-05-4P, 7-Chloro-4,8-dimethyl-2-piperazin-1-yl-quinoline 326481-06-5P, 7-Chloro-4,8-dimethyl-2-piperazin-1-yl-quinoline oxalate 326481-07-6P, 7-Chloro-4,8-dimethyl-2-piperazin-1-yl-quinoline formate 326481-08-7P, 2,7-Dichloro-4,8-dimethyl-quinoline 326481-12-3P 326481-13-4P 326481-14-5P 326481-15-6P 326481-16-7P 326481-17-8P 326481-19-0P 326481-20-3P 326481-22-5P 326481-23-6P

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 326481-90-7P 326481-94-1P 326481-97-4P 326482-00-2P 326482-02-4P  
 326482-05-7P 326482-10-4P 326482-13-7P 326482-15-9P 326482-19-3P  
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 3'-(5-Bromo-2-methoxybenzylsulfanyl)-3,4,5,6-tetrahydro-2H-  
 [1,2']bipyrazinyl 326482-30-8P 326482-31-9P 326482-33-1P  
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(MC4-R binding compound; preparation of aryl-substituted  
 tetrahydropyrimidines  
 and related compds. as melanocortin-4 receptor binding compds. for  
 treatment of pigmentation, bone, and weight loss disorders)

IT 7440-70-2, Calcium, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (depletion in bone; preparation of aryl-substituted tetrahydropyrimidines  
 and related compds. as melanocortin-4 receptor binding compds. for  
 treatment of pigmentation, bone, and weight loss disorders)

L75 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:158387 HCAPLUS Full-text

DOCUMENT NUMBER: 136:210551

TITLE: Method of treating hyperproliferative diseases using  
active vitamin D analogues

INVENTOR(S): Bishop, Charles W.; Mazess, Richard B.

PATENT ASSIGNEE(S): Bone Care International, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U.S.  
Ser. No. 596,149.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 20

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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10/501318

US 2002025950	A1	20020228	US 2001-891814	20010626 <--
US 6503893	B2	20030107		
US 5763429	A	19980609	US 1996-781910	19961230 <--
US 6537982	B1	20030325	US 1998-596149	19980223 <--
US 2002128240	A1	20020912	US 2001-995911	20011128 <--
CA 2450942	A1	20030103	CA 2002-2450942	20020626 <--
WO 2003000023	A2	20030103	WO 2002-US20475	20020626 <--
WO 2003000023	A3	20030731		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002322346	A1	20030108	AU 2002-322346	20020626 <--
EP 1408983	A2	20040421	EP 2002-756332	20020626 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR

CN 1520302	A	20040811	CN 2002-812881	20020626 <--
JP 2004535429	T	20041125	JP 2003-506479	20020626 <--
US 2003130242	A1	20030710	US 2003-337506	20030107 <--
US 6680309	B2	20040120		
MX 2003PA11307	A	20040608	MX 2003-PA11307	20031208 <--
US 2007043005	A1	20070222	US 2006-382887	20060511 <--

PRIORITY APPLN. INFO.:

US 1996-781910	A3	19961230 <--
US 1998-596149	A2	19980223 <--
US 1993-119895	A2	19930910 <--
US 1994-265438	A2	19940624 <--
US 1995-415488	A2	19950403 <--
US 1995-486387	A2	19950607 <--
US 2001-891814	A2	20010626 <--
US 2001-995911	A1	20011128 <--
WO 2002-US20475	W	20020626 <--

OTHER SOURCE(S): MARPAT 136:210551

ED Entered STN: 01 Mar 2002

AB Methods use hypocalcemic vitamin D analogs to inhibit the hyperproliferation of malignant or neoplastic cells without incidence of hypercalcemia. Patients with advanced androgen-independent prostate cancer were treated with 1 $\alpha$ ,24-dihydroxyvitamin D<sub>2</sub>.

IC ICM A61K031-59

INCL 514167000

CC 1-6 (Pharmacology)

ST hyperproliferative disease treatment vitamin D analog; antitumor hypocalcemic vitamin D analog; dihydroxyvitamin D<sub>2</sub> prostate cancer treatment

IT Lung, neoplasm

Prostate gland

(adenocarcinoma, inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases).

IT Uterus, neoplasm

(cervix, inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)

IT Intestine, neoplasm

(colon, inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)

IT Uterus, neoplasm

- (endometrium, inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Liver, neoplasm  
(hepatoma, inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Liver, neoplasm  
(hepatoma, metastasis, inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Cell differentiation  
(induction in malignant or neoplastic cells; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Bone, neoplasm  
Lung, neoplasm  
Ovary, neoplasm  
Pancreas, neoplasm  
Testis, neoplasm  
(inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Drug delivery systems  
(injections, i.v.; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Drug delivery systems  
(injections, intracancer; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Bone, neoplasm  
(metastasis, inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Prostate gland  
(neoplasm, inhibitors, androgen-independent; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Bladder  
Head  
Mammary gland  
Neck, anatomical  
(neoplasm, inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Lung, neoplasm  
(non-small-cell carcinoma, inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Drug delivery systems  
(oral; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Eye, neoplasm  
(retinoblastoma, inhibitors, metastasis; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Eye, neoplasm  
(retinoblastoma, inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Lung, neoplasm  
(small-cell carcinoma, inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT Head  
Lung, neoplasm  
Neck, anatomical  
(squamous cell carcinoma, inhibitors; hypocalcemic vitamin D analogs for treating hyperproliferative diseases)
- IT 51-21-8, 5-Fluorouracil 57-22-7, Vincristine 59-05-2, Methotrexate  
865-21-4, Vinblastine 1404-00-8, Mitomycin 4891-15-0, Estramustine  
phosphate 7440-06-4D, Platinum, cytotoxic compds. 7689-03-4D,  
Camptothecin, compds. 15663-27-1, Cisplatin 20830-81-3, Daunorubicin

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21679-14-1, Fludarabine 23214-92-8, Doxorubicin 25316-40-9, Adriamycin  
29069-24-7, Prednimustine 33419-42-0, Etoposide 41575-94-4,  
Carboplatin 58957-92-9, Idarubicin 61825-94-3,  
Oxaliplatin 110172-45-7, CI-973 129580-63-8, JM-216

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(coadministration with; hypocalcemic vitamin D analogs for treating  
hyperproliferative diseases)

IT 7440-70-2, Calcium, biological studies

RL: ADV (Adverse effect, including toxicity); BSU (Biological study,  
unclassified); BIOL (Biological study)

(hypocalcemic vitamin D analogs for treating hyperproliferative  
diseases)

L75 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:123598 HCAPLUS Full-text

DOCUMENT NUMBER: 136:161350

TITLE: Method of inhibiting angiogenesis associated with  
malignant and neoplastic cells using active  
vitamin D analogs

INVENTOR(S): Bishop, Charles W.; Mazess, Richard B.

PATENT ASSIGNEE(S): Bone Care International, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U.S.  
Ser. No. 596,149.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 20

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002019375	A1	20020214	US 2001-891805	20010626 <--
US 6573256	B2	20030603		
US 5763429	A	19980609	US 1996-781910	19961230 <--
US 6537982	B1	20030325	US 1998-596149	19980223 <--
PRIORITY APPLN. INFO.:			US 1996-781910	A3 19961230 <--
			US 1998-596149	A2 19980223 <--
			US 1993-119895	A2 19930910 <--
			US 1994-265438	A2 19940624 <--
			US 1995-415488	A2 19950403 <--
			US 1995-486387	A2 19950607 <--

OTHER SOURCE(S): MARPAT 136:161350

ED Entered STN: 15 Feb 2002

AB Methods are disclosed which use active vitamin D analogs for the inhibition of  
angiogenesis associated with malignant and neoplastic cells. Methods comprise  
the application of an effective amount of a hypocalcemic hydroxyvitamin D  
compound to inhibit the angiogenesis of malignant cells, induce the apoptosis  
of malignant cells, and regress the growth of tumor cells.

IC ICM A61K031-59

INCL 514167000

CC 1-6 (Pharmacology)

IT Lung, neoplasm

(adenocarcinoma, inhibitors; hydroxyvitamin D compds. for inhibition of  
tumor-associated angiogenesis, and use with other agents)

IT Microtubule

(anti-microtubule agents; hydroxyvitamin D compds. for inhibition of  
tumor-associated angiogenesis, and use with other agents)

IT Nutrients

(antinutrients; hydroxyvitamin D compds. for inhibition of



tumor-associated angiogenesis, and use with other agents)

IT Antitumor agents  
(bladder carcinoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

IT Antitumor agents  
(bone; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

IT Bladder  
(carcinoma, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

IT Uterus, neoplasm  
(cervix, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

IT Antitumor agents  
(cervix; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

IT Intestine, neoplasm  
(colon, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

IT Antitumor agents  
(colon; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

IT Uterus, neoplasm  
(endometrium, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

IT Antitumor agents  
(endometrium; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

IT Gene, animal  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(growth hormone; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)

IT Antitumor agents  
(head and neck squamous cell carcinoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)

IT Antitumor agents  
(head; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

IT Liver, neoplasm  
(hepatoma, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)

IT Antitumor agents  
(hepatoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)

IT Angiogenesis inhibitors  
Antitumor agents  
(hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

IT Alkylating agents, biological  
Antibiotics  
Apoptosis  
Cytotoxic agents  
Human  
(hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)

IT Gene expression  
Vitamin D receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(hydroxyvitamin D compds. for inhibition of tumor-associated

- angiogenesis, and use with other agents)
- IT Anthracyclines  
Taxanes  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT Bone, neoplasm  
Lung, neoplasm  
Ovary, neoplasm  
Pancreas, neoplasm  
Testis, neoplasm  
(inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Drug delivery systems  
(injections, i.v.; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Drug delivery systems  
(injections; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Lung, neoplasm  
(large-cell carcinoma, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT Antitumor agents  
(lung adenocarcinoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT Antitumor agents  
(lung large-cell carcinoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT Antitumor agents  
(lung non-small-cell carcinoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT Antitumor agents  
(lung small-cell carcinoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT Antitumor agents  
(lung squamous cell carcinoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT Antitumor agents  
(lung; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Antitumor agents  
(lymphocytic leukemia; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Antitumor agents  
(lymphoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Antitumor agents  
(mammary gland; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Thyroid gland, neoplasm  
(medullary carcinoma, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Antitumor agents  
(melanoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Antitumor agents  
(multiple myeloma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

- IT Antitumor agents  
(myelogenous leukemia; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Antitumor agents  
(neck; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Head  
Mammary gland  
Neck, anatomical  
Prostate gland  
(neoplasm, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Lung, neoplasm  
(non-small-cell carcinoma, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT Drug delivery systems  
(oral; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Antitumor agents  
(ovary; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Antitumor agents  
(pancreas; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Antitumor agents  
(prostate gland; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Eye, neoplasm  
(retinoblastoma, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Antitumor agents  
(retinoblastoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Antitumor agents  
(sarcoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Lung, neoplasm  
(small-cell carcinoma, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT Antitumor agents  
(soft tissue; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Animal tissue  
(soft, neoplasm, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Head  
Lung, neoplasm  
Neck, anatomical  
(squamous cell carcinoma, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT Antitumor agents  
(squamous cell carcinoma; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Antitumor agents  
(testis; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT Carcinoma

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(thyroid medullary, inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)

- IT 9002-72-6, Growth hormone  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(gene; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT 1406-16-2D, Vitamin D, hydroxy derivs. 54573-75-0, 1 $\alpha$ -Hydroxyvitamin D2 60133-18-8, 1 $\alpha$ ,25-Dihydroxyvitamin D2 124043-51-2, 1 $\alpha$ ,24-Dihydroxyvitamin D2 131249-38-2, 1 $\alpha$ ,25-Dihydroxyvitamin D4 143032-85-3, 1 $\alpha$ -Hydroxyvitamin D4 157893-62-4, 1 $\alpha$ ,24-Dihydroxyvitamin D4  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT 19356-17-3, 25-Hydroxyvitamin D3 32222-06-3, 1 $\alpha$ ,25-Dihydroxyvitamin D3  
RL: PAC (Pharmacological activity); BIOL (Biological study)  
(hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT 50-18-0, Cyclophosphamide 51-21-8, 5-Fluorouracil 57-22-7, Vincristine 59-05-2, Methotrexate 127-07-1, Hydroxyurea 148-82-3, Melphalan 865-21-4, Vinblastine 1404-00-8, Mitomycin 4891-15-0, Estramustine phosphate 7440-06-4D, Platinum, compds. 7689-03-4, Camptothecin 7689-03-4D, Camptothecin, derivs. 15663-27-1, Cisplatin 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 23214-92-8, Doxorubicin 25316-40-9, Adriamycin 29069-24-7, Prednimustine 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin 58957-92-9, Idarubicin 61825-94-3, Oxaliplatin 110172-45-7, CI-973 114977-28-5, Docetaxel 129580-63-8, JM-216 156316-85-7, 1 $\alpha$ ,24(S)-Dihydroxyvitamin D2 156316-86-8  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)
- IT 7440-70-2, Calcium, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(hypocalcemic hydroxyvitamin D compds.; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis)
- IT 80449-01-0, Topoisomerase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; hydroxyvitamin D compds. for inhibition of tumor-associated angiogenesis, and use with other agents)

L75 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:461293 HCAPLUS Full-text

DOCUMENT NUMBER: 137:37649

TITLE: Oxalic acid or oxalate  
compositions and methods for vascular disorders,  
diseases, and calcerous conditions

INVENTOR(S): Hart, Francis J.

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 39 pp., Cont.-in-part of U.S. 6,133,318.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

10/501318

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6407141	B1	20020618	US 2000-535572	20000327 <--
US 6133317	A	20001017	US 1996-629538	19960409 <--
US 6133318	A	20001017	US 1998-14943	19980128 <--
PRIORITY APPLN. INFO.:			US 1995-6785P	P 19951115 <--
			US 1996-629538	A2 19960409 <--
			US 1997-36983P	P 19970129 <--
			US 1998-14943	A2 19980128 <--

ED Entered STN: 20 Jun 2002

AB A single medicine oxalic acid or oxalate compns., or "magic bullet" and methods of treatment and prevention of warm-blooded animals including humans and pets for vascular diseases, disorders, and calcerous conditions, chemoprevention of vascular diseases, disorders, and calcerous conditions, is provided. The composition includes at least one therapeutically effective form of oxalic acid or oxalate selected from oxalic acid ester, lactone or salt form and oxalate including sodium oxalate, oxalic acid dihydrate, anhydrous oxalic acid, and oxamide, natural or processed foods including molds, plants or vegetables containing oxalic acid or oxalate, beverages, liqs. or juices containing oxalic acid or oxalate, additives containing oxalic acid or oxalate, and combinations thereof. The compns. may also contain a pharmaceutically acceptable carrier or diluent for the therapeutically effective form of oxalic acid or oxalate. Methods are provided including the steps of periodically administering, by topical, oral, or parenteral application, a therapeutically effective dosage of a composition including at least one therapeutically effective form of oxalic acid or oxalate in less than a lethal dosage and improving chemotherapy by reducing the intake of oxalic acid or oxalate blockers such as citric acid, ascorbic acid (vitamin C), pyridoxine hydrochloride (vitamin B6), calcium, alc., resins, clays, foods containing calcium, beverages containing alc., citric or ascorbic acid, red meat or white meat of fowl containing pyridoxine hydrochloride, or other foods, nutritional supplements or beverages containing oxalic acid or oxalate blockers. For example, a nutritional supplement or multivitamin, multi-mineral tablet contained a small quantity of oxalic acid, preferably 500 mg or less of oxalic acid, together with conventional ingredients such as vitamins and minerals.

IC ICM A61K031-194  
ICS A61K031-225

INCL 514574000

CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1, 17, 18, 62

ST oxalate pharmaceutical nutritional supplement vascular disease;  
cardiovascular agent oxalic acid pharmaceutical  
nutritional supplement

IT Imaging  
(NMR, oxalic acid decomposition or reduction by;  
oxalic acid or oxalate compns. and methods  
for treatment and prevention of vascular and brain diseases and  
calcerous conditions)

IT Antiarteriosclerotics  
(antiatherosclerotics; oxalic acid or  
oxalate compns. and methods for treatment and prevention of  
vascular and brain diseases and calcerous conditions)

IT Infection  
(bacterial; oxalic acid or oxalate  
compns. and methods for treatment and prevention of vascular and brain  
diseases and calcerous conditions)

IT Drug delivery systems  
(capsules, soft; oxalic acid or oxalate  
compns. and methods for treatment and prevention of vascular and brain

- diseases and calcerous conditions)
- IT Drug delivery systems  
(capsules; oxalic acid or oxalate compns.  
and methods for treatment and prevention of vascular and brain diseases  
and calcerous conditions)
- IT Beverages  
(carbonated; oxalic acid or oxalate  
compns. and reduction of intake of oxalate blockers for treatment  
and prevention of vascular and brain diseases and calcerous conditions)
- IT Daucus carota  
Fruit and vegetable juices  
(carrot juice; oxalic acid or oxalate  
compns. and methods for treatment and prevention of vascular and brain  
diseases and calcerous conditions)
- IT Meat  
(chicken; oxalic acid or oxalate compns.  
and reduction of intake of oxalate blockers for treatment and  
prevention of vascular and brain diseases and calcerous conditions)
- IT Digestive tract  
(damage; oxalic acid or oxalate compns.  
and methods for treatment and prevention of vascular and brain diseases  
and calcerous conditions)
- IT Feed  
(dog; oxalic acid or oxalate compns. and  
methods for treatment and prevention of vascular and brain diseases and  
calcerous conditions)
- IT Drug delivery systems  
(drops; oxalic acid or oxalate compns.  
and methods for treatment and prevention of vascular and brain diseases  
and calcerous conditions)
- IT Magnetic field  
Radiation  
(elimination of use of; oxalic acid or  
oxalate compns. and methods for treatment and prevention of  
vascular and brain diseases and calcerous conditions)
- IT Heart, disease  
Inflammation  
(endocarditis; oxalic acid or oxalate  
compns. and methods for treatment and prevention of vascular and brain  
diseases and calcerous conditions)
- IT Kidney, disease  
(failure; oxalic acid or oxalate compns.  
and methods for treatment and prevention of vascular and brain diseases  
and calcerous conditions)
- IT Canis familiaris  
(food; oxalic acid or oxalate compns. and  
methods for treatment and prevention of vascular and brain diseases and  
calcerous conditions)
- IT Drug delivery systems  
(gels; oxalic acid or oxalate compns. and  
methods for treatment and prevention of vascular and brain diseases and  
calcerous conditions)
- IT Alcoholic beverages  
(gin; oxalic acid or oxalate compns. and  
reduction of intake of oxalate blockers for treatment and  
prevention of vascular and brain diseases and calcerous conditions)
- IT Temperature effects, biological  
(heat, oxalic acid decomposition or reduction by;  
oxalic acid or oxalate compns. and methods  
for treatment and prevention of vascular and brain diseases and

- calcerous conditions)
- IT Digestive tract, disease  
(indigestion; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Cardiovascular system, disease  
(infections; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Drug delivery systems  
(inhalants; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Drug delivery systems  
(injections, i.v.; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Drug delivery systems  
(injections, s.c.; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Drug delivery systems  
(injections; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Kidney, disease  
(injury; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Drug delivery systems  
(liqs.; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Drug delivery systems  
(lozenges; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Radiography  
(mammog., oxalic acid decomposition or reduction by; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Drug delivery systems  
(nasal; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Drug delivery systems  
(oral; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Blood analysis  
Urine analysis  
(oxalate detection in, test kit for; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Blood  
(oxalate in; oxalic acid or oxalate compns. and methods for treatment and prevention of vascular and brain diseases and calcerous conditions)
- IT Urine

- (oxalate of; oxalic acid or  
oxalate compns. and methods for treatment and prevention of  
vascular and brain diseases and calcerous conditions)
- IT Kidney, disease  
(oxalate-induced; oxalic acid or  
oxalate compns. and methods for treatment and prevention of  
vascular and brain diseases and calcerous conditions)
- IT Electromagnetic wave  
Microwave  
Radiotherapy  
Tomography  
(oxalic acid decomposition or reduction by; oxalic  
acid or oxalate compns. and methods for treatment and  
prevention of vascular and brain diseases and calcerous conditions)
- IT Alcoholic beverages  
Allium sativum  
Allium schoenoprasum  
Alzheimer's disease  
Animals  
Anti-Alzheimer's agents  
Antiartherosclerotics  
Antibacterial agents  
Antimicrobial agents  
Antitumor agents  
Antitumor agents  
Antiviral agents  
Apium graveolens  
Beta vulgaris  
Beverages  
Blood vessel, disease  
Brain, disease  
Bread  
Cardiovascular agents  
Cereal (grain)  
Daucus carota  
Diarrhea  
Dietary supplements  
Embryophyta  
Flavoring materials  
Food  
Food additives  
Fruit and vegetable juices  
Human  
Liquids  
Mold (fungus)  
Mouthwashes  
Pepper (spice)  
Pet animal  
Petroselinum crispum  
Physiological saline solutions  
Plants  
Preservatives  
Spinacia oleracea  
Tomato juice  
Vegetable  
(oxalic acid or oxalate compns. and  
methods for treatment and prevention of vascular and brain diseases and  
calcerous conditions)
- IT Mineral elements, biological studies  
Vitamins



RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (oxalic acid or oxalate compns. and  
 methods for treatment and prevention of vascular and brain diseases and  
 calcerous conditions)

- IT Beer
  - Cocos nucifera
  - Dairy products
  - Fruit
  - Wine
    - (oxalic acid or oxalate compns. and reduction  
 of intake of oxalate blockers for treatment and prevention of  
 vascular and brain diseases and calcerous conditions)
- IT Alcohols, biological studies
  - Clays, biological studies
  - Resins
- RL: BSU (Biological study, unclassified); BIOL (Biological study)
  - (oxalic acid or oxalate compns. and reduction  
 of intake of oxalate blockers for treatment and prevention of  
 vascular and brain diseases and calcerous conditions)
- IT Drug delivery systems
  - (parenterals; oxalic acid or oxalate  
 compns. and methods for treatment and prevention of vascular and brain  
 diseases and calcerous conditions)
- IT Drug delivery systems
  - (pellets; oxalic acid or oxalate compns.  
 and methods for treatment and prevention of vascular and brain diseases  
 and calcerous conditions)
- IT Meat
  - (pheasant; oxalic acid or oxalate compns.  
 and reduction of intake of oxalate blockers for treatment and  
 prevention of vascular and brain diseases and calcerous conditions)
- IT Drug delivery systems
  - (powders; oxalic acid or oxalate compns.  
 and methods for treatment and prevention of vascular and brain diseases  
 and calcerous conditions)
- IT Injury
  - (renal; oxalic acid or oxalate compns.  
 and methods for treatment and prevention of vascular and brain diseases  
 and calcerous conditions)
- IT Drug delivery systems
  - (sublingual; oxalic acid or oxalate  
 compns. and methods for treatment and prevention of vascular and brain  
 diseases and calcerous conditions)
- IT Drug delivery systems
  - (suppositories; oxalic acid or oxalate  
 compns. and methods for treatment and prevention of vascular and brain  
 diseases and calcerous conditions)
- IT Drug delivery systems
  - (tablets; oxalic acid or oxalate compns.  
 and methods for treatment and prevention of vascular and brain diseases  
 and calcerous conditions)
- IT Drug delivery systems
  - (topical; oxalic acid or oxalate compns.  
 and methods for treatment and prevention of vascular and brain diseases  
 and calcerous conditions)
- IT Drug delivery systems
  - (transdermal; oxalic acid or oxalate  
 compns. and methods for treatment and prevention of vascular and brain  
 diseases and calcerous conditions)
- IT Meat

(turkey; oxalic acid or oxalate compns.  
and reduction of intake of oxalate blockers for treatment and  
prevention of vascular and brain diseases and calcerous conditions)

## IT Infection

(viral; oxalic acid or oxalate  
compns. and methods for treatment and prevention of vascular and brain  
diseases and calcerous conditions)

## IT Alcoholic beverages

(vodka; oxalic acid or oxalate compns.  
and reduction of intake of oxalate blockers for treatment and  
prevention of vascular and brain diseases and calcerous conditions)

## IT 7647-14-5, Sodium chloride, biological studies

RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)

(oxalic acid or oxalate compns. and  
methods for treatment and prevention of vascular and brain diseases and  
calcerous conditions)

## IT 62-76-0, Sodium oxalate 144-62-7, Oxalic

acid, biological studies 144-62-7D, Oxalic  
acid, esters 144-62-7D, Oxalic acid,  
lactones, biological studies 144-62-7D, Oxalic  
acid, salts 471-46-5, Oxamide 6153-56-6, Oxalic  
acid dihydrate

RL: FFD (Food or feed use); PAC (Pharmacological activity); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)

(oxalic acid or oxalate compns. and  
methods for treatment and prevention of vascular and brain diseases and  
calcerous conditions)

## IT 50-81-7, Vitamin C, biological studies 58-56-0, Pyridoxine hydrochloride

65-23-6, Pyridoxine 77-92-9, Citric acid, biological studies

7440-70-2, Calcium, biological studies 8059-24-3, Vitamin B6

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(oxalic acid or oxalate compns. and reduction  
of intake of oxalate blockers for treatment and prevention of  
vascular and brain diseases and calcerous conditions)

REFERENCE COUNT: 92 THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:136991 HCAPLUS Full-text

DOCUMENT NUMBER: 134:198075

TITLE: Triglyceride-free compositions and methods for  
enhanced absorption of hydrophilic therapeutic agents

INVENTOR(S): Patel, Mahesh V.; Chen, Feng-Jing

PATENT ASSIGNEE(S): Lipocine, Inc., USA

SOURCE: PCT Int. Appl., 113 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 13

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012155	A1	20010222	WO 2000-US18807	20000710 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,				
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,				
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,				
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,				
ZA, ZW				

10/501318

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6309663	B1	20011030	US 1999-375636	19990817 <--
CA 2380642	A1	20010222	CA 2000-2380642	20000710 <--
EP 1210063	A1	20020605	EP 2000-947184	20000710 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506476	T	20030218	JP 2001-516502	20000710 <--
NZ 517659	A	20041224	NZ 2000-517659	20000710 <--
AU 780877	B2	20050421	AU 2000-60838	20000710 <--
US 2001024658	A1	20010927	US 2000-751968	20001229 <--
US 6458383	B2	20021001		

PRIORITY APPLN. INFO.:

US 1999-375636	A	19990817 <--
WO 2000-US18807	W	20000710 <--

ED Entered STN: 25 Feb 2001

AB The present invention relates to triglyceride-free pharmaceutical compns., pharmaceutical systems, and methods for enhanced absorption of hydrophilic therapeutic agents. The compns. and systems include an absorption enhancing carrier, where the carrier is formed from a combination of at least two surfactants, at least one of which is hydrophilic. A hydrophilic therapeutic agent can be incorporated into the composition, or can be co-administered with the composition as part of a pharmaceutical system. The invention also provides methods of treatment with hydrophilic therapeutic agents using these compns. and systems. For example, when a composition containing Cremophor RH40 0.30, Arlacel 186 0.20, Na taurocholate 0.18, and propylene glycol 0.32 g, resp., was used, the relative absorption of PEG 4000 as a model macromol. drug was enhanced by 991%.

IC ICM A61K009-00

ICS A61K009-14; A61K009-16; A61K009-20; A61K009-22; A61K009-28;  
A61K009-48

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

IT Analgesics

Anthelmintics

Anti-inflammatory agents

Antianginal agents

Antiarrhythmics

Antiasthmatics

Antibacterial agents

Anticoagulants

Anticonvulsants

Antidepressants

Antidiabetic agents

Antifoaming agents

Antihistamines

Antihypertensives

Antimalarials

Antimigraine agents

Antiparkinsonian agents

Antipsychotics

Antitumor agents

Antitussives

Antiviral agents

Anxiolytics

Blood serum

Buffers

Chelating agents

Compression

Diuretics

Drug delivery systems  
 Encapsulation  
 Extrusion, nonbiological  
 Flavoring materials  
 Fungicides  
 Hypnotics and Sedatives  
 Immunosuppressants  
 Inotropics  
 Molding  
 Muscarinic antagonists  
 Muscle relaxants  
 Nervous system stimulants  
 Nutrients  
 Peptidomimetics  
 Plasticizers  
 Preservatives  
 Protozoacides  
 Solubilizers  
 Spheronization  
 Surfactants  
 Vaccines

(compsn. for enhanced absorption of hydrophilic drugs using combination of surfactants)

IT Acrylic polymers, biological studies  
 Alcohols, biological studies  
 Amides, biological studies  
 Amino acids, biological studies  
 Carbohydrates, biological studies  
 Corticosteroids, biological studies  
 Cytokines  
 Diglycerides  
 Elastins  
 Enkephalins  
 Esters, biological studies  
 Fatty acids, biological studies  
 Genetic element  
 Glycerides, biological studies  
 Glycosides  
 Interleukin 2  
 Interleukin 3  
 Lecithins  
 Lysophosphatidic acids  
 Lysophosphatidylcholines  
 Lysophosphatidylethanolamines  
 Lysophosphatidylserines  
 Macromolecular compounds  
 Nucleic acids  
 Nucleosides, biological studies  
 Nucleotides, biological studies  
 Oligonucleotides  
 Peptides, biological studies  
 Phosphatidic acids  
 Phosphatidylcholines, biological studies  
 Phosphatidylethanolamines, biological studies  
 Phosphatidylglycerols  
 Phosphatidylserines  
 Phospholipids, biological studies  
 Platelet-derived growth factors  
 Polyoxyalkylenes, biological studies  
 Proteins, general, biological studies

Sex hormones  
 Shellac  
 Sterols  
 Sulfonic acids, biological studies  
 Tannins  
 Toxoids

Tumor necrosis factors

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (compns. for enhanced absorption of hydrophilic drugs using combination of surfactants)

IT Tumor necrosis factor receptors

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (fusion protein with antibody Fc fragment; compns. for enhanced absorption of hydrophilic drugs using combination of surfactants)

IT Drug delivery systems

(oral; compns. for enhanced absorption of hydrophilic drugs using combination of surfactants)

IT Japanese encephalitis virus

Mycobacterium BCG

Neisseria meningitidis

Rabies

Rotavirus

Streptococcus pneumoniae

Typhoid fever

(vaccines; compns. for enhanced absorption of hydrophilic drugs using combination of surfactants)

IT 50-21-5, Lactic acid, biological studies 50-21-5D, Lactic acid, acyl esters 50-56-6, Oxytocin, biological studies 50-70-4, Sorbitol, biological studies 50-81-7, Ascorbic acid, biological studies 51-15-0, Pralidoxime chloride 51-43-4, Epinephrine 51-55-8, Atropine, biological studies 51-60-5, Neostigmine methyl sulfate 52-24-4, Thiotepe 53-79-2, Puromycin 56-81-5, Glycerol, biological studies 57-10-3, Palmitic acid, biological studies 57-11-4, Stearic acid, biological studies 57-13-6, Urea, biological studies 57-22-7, Vincristine 57-55-6, Propylene glycol, biological studies 57-55-6D, Propylene glycol, ethers 57-64-7, Physostigmine salicylate 57-88-5, Cholesterol, biological studies 57-94-3, Tubocurarine chloride 59-05-2, Methotrexate 60-00-4, EDTA, biological studies 60-00-4D, EDTA, conjugates with antipain and chitosan 60-31-1, Acetylcholine chloride 60-33-3, Linoleic acid, biological studies 62-31-7, Dopamine hydrochloride 63-91-2, Phenylalanine, biological studies 64-18-6, Formic acid, biological studies 64-19-7, Acetic acid, biological studies 65-28-1, Phentolamine mesylate 65-85-0, Benzoic acid, biological studies 66-71-7, 1,10-Phenanthroline 67-42-5, EGTA 68-11-1, Thioglycolic acid, biological studies 68-19-9, Vitamin B12 69-65-8, Mannitol 69-72-7, Salicylic acid, biological studies 69-79-4D, Maltose, alkyl esters 69-93-2, Uric acid, biological studies 70-51-9, Deferoxamine 71-27-2, Suxamethonium chloride 74-89-5, Methanamine, biological studies 75-75-2, Methanesulfonic acid 77-19-0, Dicyclomine 77-92-9, Citric acid, biological studies 77-92-9D, Citric acid, glycerides 79-09-4, Propionic acid, biological studies 79-10-7, Acrylic acid, biological studies 79-10-7D, Acrylic acid, polymers 81-24-3, Taurocholic acid 81-25-4, Cholic acid 83-44-3, Deoxycholic acid 87-69-4, Tartaric acid, biological studies 87-69-4D, Tartaric acid, glycerides 89-57-6, Mesalamine 89-65-6, Isoascorbic acid 101-26-8, Pyridostigmine bromide 102-71-6, Triethanolamine, biological studies 104-15-4, p-Toluenesulfonic acid, biological studies 107-15-3, Ethylenediamine, biological studies 107-21-1, Ethylene glycol, biological studies 107-92-6, Butyric acid, biological studies 110-15-6, Succinic acid, biological studies 110-16-7, Maleic acid, biological studies 110-17-8,

Fumaric acid, biological studies 110-27-0, Isopropyl myristate 111-62-6, Ethyl oleate 112-80-1, Oleic acid, biological studies 114-07-8, Erythromycin 114-80-7, Neostigmine bromide 115-77-5, Pentaerythritol, biological studies 121-44-8, Triethylamine, biological studies 122-20-3, Triisopropanolamine 124-04-9, Adipic acid, biological studies 124-07-2, Caprylic acid, biological studies 128-13-2, Ursodeoxycholic acid 129-06-6, Warfarin sodium 131-49-7, Diatrizoate meglumine 138-36-3, p-Bromobenzenesulfonic acid 140-64-7, Pentamidine isethionate 141-22-0, Ricinoleic acid 141-43-5, Ethanolamine, biological studies 142-62-1, Caproic acid, biological studies 142-91-6, Isopropyl palmitate 143-07-7, Lauric acid, biological studies 143-07-7D, Lauric acid, Macrogol glycerides 144-55-8, Sodium hydrogen carbonate, biological studies 144-62-7, Oxalic acid, biological studies 145-42-6, Sodium taurocholate 147-94-4, Cytarabine 148-24-3, 8-Quinolinol, biological studies 151-21-3, Sodium lauryl sulfate, biological studies 151-41-7, Lauryl sulfate 154-21-2, Lincomycin 155-97-5, Pyridostigmine 299-42-3, Ephedrine 334-48-5, Capric acid 360-65-6, Glycodeoxycholic acid 434-13-9, Lithocholic acid 463-40-1, Linolenic acid 463-79-6, Carbonic acid, biological studies 471-34-1, Calcium carbonate, biological studies 474-25-9, Chenodeoxycholic acid 475-31-0, Glycocholic acid 516-35-8, Taurochenodeoxycholic acid 516-50-7, Taurodeoxycholic acid 526-95-4, Gluconic acid 541-15-1D, Carnitine, fatty acid ester salts 544-35-4, Ethyl linoleate 544-63-8, Myristic acid, biological studies 577-11-7, Sodium docusate 616-91-1, N-Acetylcysteine 640-79-9, Glycochenodeoxycholic acid 665-66-7, Amantadine hydrochloride 737-31-5, Diatrizoate sodium 863-57-0, Sodium glycocholate 865-21-4, Vinblastin 1002-62-6, Sodium caprate 1115-70-4, Metformin hydrochloride 1264-72-8, Colistin sulfate 1309-42-8, Magnesium hydroxide 1310-58-3, Potassium hydroxide, biological studies 1310-73-2, Sodium hydroxide, biological studies 1319-82-0, Aminocaproic acid 1327-43-1, Magnesium aluminum silicate 1330-80-9, Propylene glycol monooleate 1335-30-4, Aluminum silicate 1336-21-6, Ammonium hydroxide 1338-39-2, Span 20 1338-41-6, Sorbitan monostearate 1338-43-8, Span 80 1397-89-3, Amphotericin B 1403-66-3, Gentamycin 1404-90-6, Vancomycin 1405-20-5, Polymixin B sulfate 1405-37-4, Capreomycin sulfate 1405-87-4, Bacitracin 1492-18-8, Leucovorin calcium 1501-84-4, Rimantadine hydrochloride 1684-40-8, Tacrine hydrochloride 1695-77-8, Spectinomycin 1935-18-8, Palmitoyl carnitine 2016-88-8, Amiloride hydrochloride 2364-67-2, Palmitoyl carnitine 2466-77-5, Lauroyl carnitine 2646-38-0, Sodium chenodeoxycholate 2898-95-5, Sodium ursodeoxycholate 3056-17-5, Stavudine 3485-62-9, Clidinium bromide 3778-73-2, Isofosfamide 3858-83-1, P-Aminobenzamidine 4291-63-8, Cladribine 5534-95-2, Pentagastrin 6303-21-5D, Phosphinic acid, dipeptide derivs. 6493-05-6, Pentoxifylline 7087-68-5, Diisopropylethylamine 7481-89-2, Zalcitabine 7585-39-9D,  $\beta$ -Cyclodextrin, ethers with propanediol 7647-01-0, Hydrochloric acid, biological studies 7648-98-8, Ambenonium 7664-38-2, Phosphoric acid, biological studies 7664-93-9, Sulfuric acid, biological studies 7664-93-9D, Sulfuric acid, alkyl esters, salts, biological studies 7697-37-2, Nitric acid, biological studies 8007-43-0, Sorbitan sesquioleate 8068-28-8, Colistimethate sodium 9001-28-9, Factor IX 9002-01-1, Streptokinase 9002-60-2, Corticotropin, biological studies 9002-92-0, Brij 35 9002-96-4 9003-01-4D, Polyacrylic acid, conjugates with bacitracin 9003-39-8D, Polyvinylpyrrolidone, reaction products with phosphatidylethanolamine 9004-10-8, Insulin, biological studies 9004-17-5, Insulin protamine zinc 9004-32-4D, Carboxymethyl cellulose, conjugates with pepstatin 9004-34-6, Cellulose, biological studies 9004-34-6D, Cellulose, ethers, biological studies 9004-38-0, Cellulose acetate phthalate 9004-57-3, Ethyl cellulose 9004-81-3 9004-95-9,

10/501318

Polyethylene glycol cetyl ether 9004-96-0, Crodet O40 9004-98-2,  
Polyoxyethylene oleyl ether 9004-99-3 9005-00-9, Polyoxyethylene  
stearyl ether 9005-02-1, Kessco PEG 300DL 9005-07-6, Kessco PEG 1540DO  
9005-08-7 9005-32-7, Alginic acid 9005-63-4D, fatty acid esters  
9005-64-5, Tween 20 9005-65-6, Polysorbate 80 9005-66-7, Tween 40  
9005-67-8, Tween 60 9007-48-1, Plurol Oleique 9007-92-5, Glucagon,  
biological studies 9011-21-6 9012-76-4, Chitosan 9012-76-4D,  
Chitosan, conjugates with antipain and EDTA 9015-68-3, Asparaginase  
9034-40-6, Gonadotropin releasing hormone 9035-81-8, Trypsin inhibitor  
9036-19-5 9039-53-6, Urokinase 9041-93-4, Bleomycin sulfate  
9050-31-1, Hydroxypropylmethyl cellulose phthalate 9062-90-2 9063-46-1  
9076-44-2, Chymostatin 9078-38-0, Soybean trypsin inhibitor 9087-70-1,  
Pancreatic trypsin inhibitor 10034-85-2, Hydriodic acid 10035-10-6,  
Hydrobromic acid, biological studies 10041-19-7D, derivs. 10043-35-3,  
Boric acid, biological studies 10596-23-3 11000-17-2, Vasopressin  
11061-68-0, Human insulin 11140-04-8, Imwitor 988 12584-58-6, Porcine  
insulin 12629-01-5, Human growth hormone 13265-10-6, Methscopolamine  
13284-86-1, Sodium lithocholate 13780-71-7D, Boronic acid,  
 $\alpha$ -aminoalkyl derivs. 14440-80-3, Stearoyl-2-lactylate  
14605-22-2, Tauroursodeoxycholic acid 15500-66-0, Pancuronium bromide  
15663-27-1, Cisplatin 15686-71-2, Cephalixin 15826-37-6, Cromolyn  
sodium 16679-58-6, Desmopressin 16960-16-0, Cosyntropin 17438-29-8  
18323-44-9, Clindamycin 18883-66-4, Streptozocin  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(compsn. for enhanced absorption of hydrophilic drugs using combination  
of surfactants)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2000:738879 HCAPLUS Full-text  
DOCUMENT NUMBER: 133:301197  
TITLE: Oxalic acid or oxalate  
compositions and methods for bacterial, viral  
, and other diseases or conditions  
INVENTOR(S): Hart, Francis J.  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S., 50 pp., Cont.-in-part of U. S. Ser. No. 629,538.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6133318	A	20001017	US 1998-14943	19980128 <--
US 6133317	A	20001017	US 1996-629538	19960409 <--
US 6407141	B1	20020618	US 2000-535572	20000327 <--
PRIORITY APPLN. INFO.:			US 1995-6785P	P 19951115 <--
			US 1996-629538	A2 19960409 <--
			US 1997-36983P	P 19970129 <--
			US 1998-14943	A2 19980128 <--

ED Entered STN: 19 Oct 2000

AB A single medicine oxalic acid or oxalate or "magic bullet" and method for  
treatment or prevention of infectious or pathogenic microbial, bacterial,  
viral and other diseases in warm-blooded animals, including humans and pets,  
is provided. A composition includes at least one therapeutically effective  
form of oxalic acid or oxalate selected from ester, lactone or salt form  
including sodium oxalate, oxalic acid dihydrate, anhydrous oxalic acid,

oxamide, and oxalate salts, natural or processed foods including molds, plants or vegetables containing oxalic acid or oxalate, beverages, liqs. or juices containing oxalic acid or oxalate, additives containing oxalic acid or oxalate, and combinations thereof. The composition may also contain a pharmaceutically acceptable carrier or diluent for the therapeutically effective form of oxalic acid or oxalate. Methods are provided including the steps of periodically administering, by topical, oral, or parenteral application, a therapeutically effective dosage of a composition including at least one therapeutically effective form of oxalic acid or oxalate and improving chemotherapy reducing the intake of oxalic acid or oxalate blockers such as citric acid, ascorbic acid (vitamin C), pyridoxine hydrochloride (vitamin B6), calcium, alc., resins, clays, foods containing calcium, beverages containing alc., citric acid, or ascorbic acid, red meat or white meat of fowl containing pyridoxine hydrochloride, or other foods nutritional supplements or beverages containing oxalic acid or oxalate blockers.

- IC ICM A61K031-194
- ICS A61K031-225
- INCL 514574000
- CC 63-6 (Pharmaceuticals)
- Section cross-reference(s): 1, 17, 18, 62
- ST oxalate antitumor antibacterial antiviral nutrient food
- IT Brain, disease
- Prion diseases
- (Creutzfeldt-Jakob; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Imaging
- (NMR; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases and protection from radiation)
- IT Streptococcus
- (Viridans-group; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Actinomyces
- (actinomycosis from; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Bacilli
- (anaerobic; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Bacillus anthracis
- (anthrax from; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Antiarteriosclerotics
- (antiatherosclerotics; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Food
- (aqueous; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Tomography
- (axial, computerized; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases and protection from radiation)
- IT Bartonella
- (bartonellosis from; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Antitumor agents
- Antitumor agents
- (brain; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems



- (capsules; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Fruit and vegetable juices  
Fruit and vegetable juices  
(carrot juice; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)
- IT Uterus, neoplasm  
Uterus, neoplasm  
(cervix, inhibitors; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Antitumor agents  
(cervix; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Meat  
(chicken; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)
- IT Digestive tract  
(disease, oxalate-induced; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)
- IT Nervous system  
(disease, viral; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Blood  
(disease; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems  
(drops; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Plant (Embryophyta)  
(edible; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)
- IT Treponema  
(endemic treponematosi from; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Intestine, disease  
(enterocolitis; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Cosmetics  
(exfoliate; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Kidney, disease  
(failure, oxalate-induced; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)
- IT Necrosis  
(gas gangrene; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems  
(gels; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Alcoholic beverages  
(gin; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)
- IT Bacilli

- (gram-neg.; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Bacilli  
(gram-pos.; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems  
(granules; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Petrolatum  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hydrophilic; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Respiratory tract  
(infection, viral; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems  
(inhalants; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Brain, neoplasm  
Brain, neoplasm  
(inhibitors; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems  
(injections, i.v.; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems  
(injections, s.c.; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems  
(injections; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Kidney, disease  
(injury, oxalate-induced; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)
- IT Carrot  
Carrot  
(juice; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)
- IT Leptospira  
(leptospirosis from; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems  
(liqs.; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Listeria monocytogenes  
(listeriosis from; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems  
(lotions; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems  
(lozenges; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Antitumor agents  
(mammary gland; oxalate compns. for prevention and treatment

- of cancer, microbial infections and other diseases)
- IT Radiography
  - (mammog.; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases and protection from radiation)
- IT Burkholderia pseudomallei
  - (melioidosis from; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems
  - (microcapsules; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems
  - (nasal sprays; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems
  - (nasal; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Mammary gland
  - Mammary gland
    - (neoplasm, inhibitors; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Clostridium
  - (of gas gangrene; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Colorimetry
  - (of oxalate; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems
  - (ointments, creams; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems
  - (ointments; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Drug delivery systems
  - (oral; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Ear
  - (otitis; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)
- IT Bakers' yeast
- Beer
- Blood analysis
- Bread
- Carrot
- Cereal (grain)
- Chive (*Allium schoenoprasum*)
- Coconut (*Cocos nucifera*)
- Dairy products
- Feed
- Fruit
- Garlic (*Allium sativum*)
- Meat
- Parsley (*Petroselinum crispum*)
- Pepper (spice)
- Preservatives
- Spinach (*Spinacia oleracea*)
- Urine analysis
- Wine

(oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)

IT Clays, biological studies

Resins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study);

USES (Uses)

(oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)

IT Smectite-group minerals

RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)

(oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)

IT Electromagnetic wave

Magnetic field

Microwave

Radiotherapy

(oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases and protection from radiation)

IT Adenoviridae

Almond (*Prunus amygdalus*)

Alphavirus

Alzheimer's disease

Anti-AIDS agents

Anti-Alzheimer's agents

Antibacterial agents

Antimicrobial agents

Antiparkinsonian agents

Antitumor agents

Antiviral agents

Arbovirus

Arenavirus

Autoimmune disease

B19 virus

Bacteremia

Bacteroides

Beet

Beverages

Biocides

Bunyavirus

Campylobacter

Cardiovascular agents

Cashew (*Anacardium occidentale*)

Cat (*Felis catus*)

Cattle

Celery (*Apium graveolens*)

Chemotherapy

*Clostridium botulinum*

*Clostridium tetani*

Cytomegalovirus

Dog (*Canis familiaris*)

Enterobacteriaceae

Enterococcus

Erysipelothrix

Filovirus

Flavivirus

Flavoring materials  
Food  
Food additives  
Fruit and vegetable juices  
Goat  
Gram-negative bacteria  
Gram-positive bacteria (Firmicutes)  
Haemophilus  
Hepatitis A virus  
Hepatitis B virus  
Hepatitis C virus  
Hepatitis delta virus  
Herpes virus B  
Hodgkin's disease  
Horse (Equus caballus)  
Human coxsackievirus  
Human echovirus  
Human herpesvirus  
Human herpesvirus 3  
Human herpesvirus 4  
Human herpesvirus 6  
Human immunodeficiency virus 1  
Human papillomavirus  
Human poliovirus  
Immunotherapy  
Influenza A virus  
Influenza B virus  
Influenza C virus  
Kale  
Leprosy  
Lyme disease  
Measles virus  
Meningitis  
Mold (fungus)  
Molluscum contagiosum virus  
Mouthwashes  
Mumps virus  
Mycobacterium  
Neisseria  
Neisseria gonorrhoeae  
Neisseria meningitidis  
Nocardia  
Orbivirus  
Osteomyelitis  
Parkinson's disease  
Parvovirus  
Peanut (Arachis hypogaea)  
Pneumonia  
Rabies virus  
Radish (Raphanus sativus)  
Reoviridae  
Respiratory syncytial virus  
Rhinovirus  
Rubella virus  
Salmonella  
Shigella  
Spirochaeta  
Staphylococcus  
Streptococcus  
Streptococcus pneumoniae

Surgery  
 Togaviridae  
 Tomato juice  
 Tuberculosis  
 Tuberculostatics  
 Vegetable  
 Walnut  
     (oxalate compns. for prevention and treatment of  
     cancer, microbial infections and other diseases)  
 IT Mineral elements, biological studies  
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
     study, unclassified); FFD (Food or feed use); THU (Therapeutic use); BIOL  
     (Biological study); USES (Uses)  
     (oxalate compns. for prevention and treatment of  
     cancer, microbial infections and other diseases)  
 IT Vitamins  
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
     study, unclassified); FFD (Food or feed use); THU (Therapeutic use); BIOL  
     (Biological study); USES (Uses)  
     (oxalate-containing; oxalate compns. for prevention and  
     treatment of cancer, microbial infections and other diseases)  
 IT Diarrhea  
     Dyspepsia  
     Kidney, disease  
     (oxalate-induced; oxalate compns. and  
     oxalate blockers for prevention and treatment of cancer  
     , microbial infections and other diseases)  
 IT Drug delivery systems  
     (parenterals; oxalate compns. for prevention and treatment of  
     cancer, microbial infections and other diseases)  
 IT Meat  
     (poultry; oxalate compns. and oxalate blockers for  
     prevention and treatment of cancer, microbial infections and  
     other diseases)  
 IT Drug delivery systems  
     (powders; oxalate compns. for prevention and treatment of  
     cancer, microbial infections and other diseases)  
 IT Respiratory tract  
     (sinusitis; oxalate compns. for prevention and treatment of  
     cancer, microbial infections and other diseases)  
 IT Drug delivery systems  
     (solns.; oxalate compns. for prevention and treatment of  
     cancer, microbial infections and other diseases)  
 IT Bread  
     (sourdough; oxalate compns. and oxalate blockers  
     for prevention and treatment of cancer, microbial infections  
     and other diseases)  
 IT Brain, disease  
     (spongiform encephalopathy; oxalate compns. for prevention  
     and treatment of cancer, microbial infections and other  
     diseases)  
 IT Beverages  
     (sports; oxalate compns. and oxalate blockers for  
     prevention and treatment of cancer, microbial infections and  
     other diseases)  
 IT Drug delivery systems  
     (sprays; oxalate compns. for prevention and treatment of  
     cancer, microbial infections and other diseases)  
 IT Drug delivery systems  
     (sticks; oxalate compns. for prevention and treatment of

cancer, microbial infections and other diseases)

IT Drug delivery systems  
(sublingual; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT Diet  
(supplements; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT Drug delivery systems  
(suppositories; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT Lupus erythematosus  
(systemic; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT Drug delivery systems  
(tablets; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT Brushes  
Brushes  
Dental materials and appliances  
Dental materials and appliances  
(toothbrushes, cleaning of; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT Drug delivery systems  
(topical; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT Drug delivery systems  
(transdermal; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT Francisella tularensis  
(tularemia from; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT Meat  
(turkey; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)

IT Drugs  
(veterinary; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT Alcoholic beverages  
(vodka; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)

IT Imaging  
(x-ray; oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases and protection from radiation)

IT 12441-09-7D, Sorbitan, esters, polyethoxylated  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Polysorbate; oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT 64-17-5, Ethanol, biological studies 65-23-6, Pyridoxine 7440-09-7, Potassium, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); USES (Uses)  
(oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)

IT 50-81-7, Ascorbic acid, biological studies 58-56-0, Pyridoxine

hydrochloride 77-92-9, biological studies 7440-70-2, Calcium, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)

IT 67-48-1, Choline chloride 91-53-2, Ethoxyquin 107-35-7, Taurine 471-34-1, Calcium carbonate, biological studies 1314-13-2, Zinc oxide, biological studies 1318-00-9, Vermiculite 1336-80-7, Iron choline citrate complex 1344-43-0, Manganous oxide, biological studies 1344-67-8, Copper chloride 5700-49-2, Ethylene diamine dihydroiodide 7447-40-7, Potassium chloride, biological studies 7487-88-9, Magnesium sulfate, biological studies 7542-09-8, Cobalt carbonate 7647-14-5, Sodium chloride, biological studies 7720-78-7, Ferrous sulfate 7757-93-9, Dicalcium phosphate 7778-18-9, Calcium sulfate 7778-80-5, Potassium sulfate, biological studies 7789-80-2, Calcium iodate 10102-18-8, Sodium selenite

RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)

(oxalate compns. and oxalate blockers for prevention and treatment of cancer, microbial infections and other diseases)

IT 144-62-7, Ethanedioic acid, biological studies

RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); MOA (Modifier or additive use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT 62-76-0, Sodium oxalate 144-62-7D, Oxalic acid, esters, lactones, or salts 471-46-5, Oxamide 6153-56-6, Oxalic acid dihydrate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

IT 57-55-6, 1,2-Propanediol, biological studies 67-64-1, Acetone, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oxalate compns. for prevention and treatment of cancer, microbial infections and other diseases)

REFERENCE COUNT: 103 THERE ARE 103 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2000:738878 HCAPLUS Full-text  
 DOCUMENT NUMBER: 133:301196  
 TITLE: Oxalic acid or oxalate composition for cancer treatment  
 INVENTOR(S): Hart, Francis J.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S., 39 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3



## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6133317	A	20001017	US 1996-629538	19960409 <--
US 6133318	A	20001017	US 1998-14943	19980128 <--
US 6407141	B1	20020618	US 2000-535572	20000327 <--
PRIORITY APPLN. INFO.:			US 1995-6785P	P 19951115 <--
			US 1996-629538	A2 19960409 <--
			US 1997-36983P	P 19970129 <--
			US 1998-14943	A2 19980128 <--

ED Entered STN: 19 Oct 2000

AB A chemopreventive composition for treatment of tumors in warm blooded animals including humans and pets is provided which includes at least one therapeutically effective form of oxalic acid or oxalate selected, for example, from oxalic acid in a free acid, ester, lactone or salt form, oxalates including sodium oxalate, a nutritional supplement containing oxalic acid or oxalate, oxalic acid dihydrate, anhydrous oxalic acid, oxamide, oxalate salts, natural or processed foods including molds, plants or vegetables containing oxalic acid or oxalate, beverages, liqs. or juices containing oxalic acid or oxalate, additives containing oxalic acid or oxalate, and combinations thereof. The composition may also contain a pharmaceutically acceptable carrier or diluent for the therapeutically effective form of oxalic acid or oxalate. A method is provided including the steps of periodically administering a therapeutically effective dosage of a composition including at least one therapeutically effective form of oxalic acid or oxalate and reducing the intake of oxalic acid or oxalate blockers such as citric acid, ascorbic acid (vitamin C), pyridoxine hydrochloride (vitamin B6), calcium, alc., resins, clays, dairy products containing calcium, fruits, coconut, beverages containing alc., ascorbic acid or citric acid, red meat or white meat of fowl containing pyridoxine hydrochloride, or other foods, nutritional supplements or beverages containing alc., citric acid, ascorbic acid, pyridoxine hydrochloride, or combinations thereof.

IC ICM A61K031-194

ICS A61K031-225

INCL 514574000

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 17, 18, 62

ST oxalate antitumor nutrient food

IT Brain, disease

Prion diseases

(Creutzfeldt-Jakob; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Antiarteriosclerotics

(antiatherosclerotics; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Food

(aqueous; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Tomography

(axial, computerized; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Prostate gland

(benign hyperplasia; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Antitumor agents

Antitumor agents  
 (brain; oxalate compns. and oxalate blockers for  
 prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
 (capsules; oxalate compns. and oxalate blockers for  
 prevention and treatment of cancer and other diseases)

IT Fruit and vegetable juices  
 Fruit and vegetable juices  
 (carrot juice; oxalate compns. and oxalate blockers  
 for prevention and treatment of cancer and other diseases)

IT Uterus, neoplasm  
 Uterus, neoplasm  
 (cervix, inhibitors; oxalate compns. and oxalate  
 blockers for prevention and treatment of cancer and other  
 diseases)

IT Antitumor agents  
 (cervix; oxalate compns. and oxalate blockers for  
 prevention and treatment of cancer and other diseases)

IT Meat  
 (chicken; oxalate compns. and oxalate blockers for  
 prevention and treatment of cancer and other diseases)

IT Digestive tract  
 (disease, oxalate-induced; oxalate compns. and  
 oxalate blockers for prevention and treatment of cancer  
 and other diseases)

IT Blood  
 (disease; oxalate compns. and oxalate blockers for  
 prevention and treatment of cancer and other diseases)

IT Parsley (*Petroselinum crispum*)  
 (dried; oxalate compns. and oxalate blockers for  
 prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
 (drops; oxalate compns. and oxalate blockers for  
 prevention and treatment of cancer and other diseases)

IT Plant (Embryophyta)  
 (edible; oxalate compns. and oxalate blockers for  
 prevention and treatment of cancer and other diseases)

IT Cosmetics  
 (exfoliant; oxalate compns. and oxalate blockers  
 for prevention and treatment of cancer and other diseases)

IT Kidney, disease  
 (failure; oxalate compns. and oxalate blockers for  
 prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
 (gels; oxalate compns. and oxalate blockers for  
 prevention and treatment of cancer and other diseases)

IT Alcoholic beverages  
 (gin; oxalate compns. and oxalate blockers for  
 prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
 (granules; oxalate compns. and oxalate blockers for  
 prevention and treatment of cancer and other diseases)

IT Petrolatum  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (hydrophilic; oxalate compns. and oxalate blockers  
 for prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
 (implants, s.c.; oxalate compns. and oxalate  
 blockers for prevention and treatment of cancer and other  
 diseases)

- IT Drug delivery systems  
(inhalants; oxalate compns. and oxalate blockers  
for prevention and treatment of cancer and other diseases)
- IT Brain, neoplasm  
Brain, neoplasm  
Skin, neoplasm  
Skin, neoplasm  
(inhibitors; oxalate compns. and oxalate blockers  
for prevention and treatment of cancer and other diseases)
- IT Drug delivery systems  
(injections, i.v.; oxalate compns. and  
oxalate blockers for prevention and treatment of cancer  
and other diseases)
- IT Drug delivery systems  
(injections, intratumoral; oxalate compns. and  
oxalate blockers for prevention and treatment of cancer  
and other diseases)
- IT Kidney, disease  
(injury, oxalate-induced; oxalate compns. and  
oxalate blockers for prevention and treatment of cancer  
and other diseases)
- IT Carrot  
Carrot  
(juice; oxalate compns. and oxalate blockers for  
prevention and treatment of cancer and other diseases)
- IT Drug delivery systems  
(liqs.; oxalate compns. and oxalate blockers for  
prevention and treatment of cancer and other diseases)
- IT Drug delivery systems  
(lotions; oxalate compns. and oxalate blockers for  
prevention and treatment of cancer and other diseases)
- IT Drug delivery systems  
(lozenges; oxalate compns. and oxalate blockers for  
prevention and treatment of cancer and other diseases)
- IT Antitumor agents  
(mammary gland; oxalate compns. and oxalate  
blockers for prevention and treatment of cancer and other  
diseases)
- IT Pheasant  
(meat; oxalate compns. and oxalate blockers for  
prevention and treatment of cancer and other diseases)
- IT Drug delivery systems  
(microcapsules; oxalate compns. and oxalate  
blockers for prevention and treatment of cancer and other  
diseases)
- IT Drug delivery systems  
(nasal; oxalate compns. and oxalate blockers for  
prevention and treatment of cancer and other diseases)
- IT Mammary gland  
Mammary gland  
(neoplasm, inhibitors; oxalate compns. and  
oxalate blockers for prevention and treatment of cancer  
and other diseases)
- IT Blood analysis  
Colorimetry  
Urine analysis  
(of oxalate; oxalate compns. and oxalate  
blockers for prevention and treatment of cancer and other  
diseases)
- IT Drug delivery systems

(ointments, creams; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
(ointments; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
(oral; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Acne  
Alcoholic beverages  
Almond (*Prunus amygdalus*)  
Alzheimer's disease  
Anti-AIDS agents  
Anti-Alzheimer's agents  
Antiparkinsonian agents  
Antitumor agents  
Antiviral agents  
Autoimmune disease  
Beer  
Beet  
Beverages  
Bread  
Cardiovascular agents  
Carrot  
Cashew (*Anacardium occidentale*)  
Cat (*Felis catus*)  
Celery (*Apium graveolens*)  
Cereal (grain)  
Chive (*Allium schoenoprasum*)  
Coconut (*Cocos nucifera*)  
Dairy products  
Dog (*Canis familiaris*)  
Feed  
Flavoring materials  
Food  
Food additives  
Fruit  
Fruit and vegetable juices  
Garlic (*Allium sativum*)  
Hodgkin's disease  
Horse (*Equus caballus*)  
Human immunodeficiency virus 1  
Intestine, disease  
Kale  
Mold (fungus)  
Mouthwashes  
Parkinson's disease  
Parvovirus  
Peanut (*Arachis hypogaea*)  
Radish (*Raphanus sativus*)  
Spinach (*Spinacia oleracea*)  
Tomato juice  
Vegetable  
Walnut  
Wine  
(oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Clays, biological studies

## Resins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); USES (Uses)

(oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Mineral elements, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Proteins, general, biological studies

RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)

(oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Electromagnetic wave

Magnetic field

Microwave

Radiotherapy

(oxalate degradation induced by; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Vitamins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oxalate-containing; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Diarrhea

Dyspepsia

(oxalate-induced; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Drug delivery systems

(parenterals; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Meat

(poultry; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Drug delivery systems

(powders; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Antitumor agents

Antitumor agents

(skin; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Drug delivery systems

(solns.; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Bread

(sourdough; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Brain, disease

(spongiform encephalopathy; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

## IT Beverages

(sports; oxalate compns. and oxalate blockers for

prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
(sprays; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
(sticks; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
(sublingual; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Diet  
(supplements; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
(suppositories; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Lupus erythematosus  
(systemic; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
(tablets; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Meat  
(tenderizers; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
(topical; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Drug delivery systems  
(transdermal; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Meat  
(turkey; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Alcoholic beverages  
(vodka; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT Imaging  
(x-ray, oxalate degradation induced by; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT 12441-09-7D, Sorbitan, esters, polyethoxylated  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Polysorbate; oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT 144-62-7, Oxalic acid, biological studies  
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); MOA (Modifier or additive use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT 64-17-5, Ethanol, biological studies 65-23-6, Pyridoxine  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); USES (Uses)  
(oxalate compns. and oxalate blockers for prevention and treatment of cancer and other diseases)

IT 62-76-0, Sodium oxalate 144-62-7D, Oxalic

10/501318

acid, esters, lactones, or salts 471-46-5, Oxamide 6153-56-6,  
Oxalic acid dihydrate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oxalate compns. and oxalate blockers for  
prevention and treatment of cancer and other diseases)

IT 50-81-7, Ascorbic acid, biological studies 58-56-0, Pyridoxine  
hydrochloride 77-92-9, Citric acid, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oxalate compns. and oxalate blockers for  
prevention and treatment of cancer and other diseases)

IT 8059-24-3, Vitamin B6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oxalate compns. and oxalate blockers for  
prevention and treatment of cancer and other diseases)

IT 7440-70-2, Calcium, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(oxalate compns. and oxalate blockers for  
prevention and treatment of cancer and other diseases)

IT 57-55-6, Propylene glycol, biological studies 67-64-1, Acetone,  
biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oxalate compns. and oxalate blockers for  
prevention and treatment of cancer and other diseases)

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 14-21 ibib ab hitind

L75 ANSWER 14 OF 21 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 1999151930 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 10029472

TITLE: Elemental analysis and clinical implications of  
calcification deposits associated with silicone breast  
implants.

AUTHOR: Raso D S; Greene W B; Kalasinsky V F; Riopel M A; Luke J L;  
Askin F B; Silverman J F; Young V L

CORPORATE SOURCE: Pathology Consultants of Central Virginia, Lynchburgh  
24501, USA.

SOURCE: Annals of plastic surgery, (1999 Feb) Vol. 42,  
No. 2, pp. 117-23.

Journal code: 7805336. ISSN: 0148-7043.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199904

ENTRY DATE: Entered STN: 4 May 1999

Last Updated on STN: 4 May 1999

Entered Medline: 16 Apr 1999

AB Calcification of the fibrous capsule surrounding silicone breast implants is a  
well-recognized occurrence that increases with time following implantation.  
These mineralized deposits potentially confound mammographic breast cancer  
surveillance already made difficult by the obscuring effects of silicone

breast implants. The authors performed elemental analysis of silicone breast implant-associated calcifications to define better their chemical composition as related to mammographic and clinical significance. Electron probe microanalysis and infrared spectroscopy revealed all of the calcification deposits to be calcium complexed with tribasic phosphate. No evidence of calcium oxalate, calcium carbonate, silicone, or talc was observed. Caution must be employed in interpreting mammograms in women with silicone breast implants as well as those who have had their silicone breast implants removed. High-density mammographic calcifications indicative of calcium phosphate associated with a silicone breast implant may represent an accepted consequence of implantation or nearby carcinoma. We recommend baseline mammography on women who have had their silicone breast implants removed to prevent unnecessary fine-needle aspiration or tissue biopsy of retained breast capsule calcifications during subsequent routine surveillance for carcinoma.

CT Check Tags: Female  
 Breast: CH, chemistry  
 Breast: UL, ultrastructure  
 Breast Diseases: ET, etiology  
 Breast Diseases: ME, metabolism  
 \*Breast Diseases: PA, pathology  
 \*Breast Implants: AE, adverse effects  
 Calcinosis: ET, etiology  
 Calcinosis: ME, metabolism  
 \*Calcinosis: PA, pathology  
 Calcium Phosphates: AN, analysis  
 Electron Probe Microanalysis  
 Humans  
 Microscopy, Electron, Scanning  
 Middle Aged  
 \*Silicone Gels: AE, adverse effects  
 Spectrophotometry, Infrared  
 CN 0 (Calcium Phosphates); 0 (Silicone Gels)

L75 ANSWER 15 OF 21 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:199535 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV200200199535  
 TITLE: Inactivation of the *Saccharomyces cerevisiae* SKY1 gene induces a specific modification of the yeast anticancer drug sensitivity profile accompanied by a mutator phenotype.  
 AUTHOR(S): Schenk, Paul W.; Boersma, Antonius W. M.; Brok, Mariel; Burger, Herman; Stoter, Gerrit; Nooter, Kees [Reprint author]  
 CORPORATE SOURCE: Department of Medical Oncology, University Hospital Rotterdam, Josephine Nefkens Building, Room Be422, 3000 DR, Rotterdam, Netherlands  
 nooter@oncd.azr.nl  
 SOURCE: Molecular Pharmacology, (March, 2002) Vol. 61, No. 3, pp. 659-666. print.  
 CODEN: MOPMA3. ISSN: 0026-895X.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 20 Mar 2002  
 Last Updated on STN: 20 Mar 2002

AB The therapeutic potential of the highly active anticancer agent cisplatin is severely limited by the occurrence of cellular resistance. A better understanding of the molecular pathways involved in cisplatin-induced cell death could potentially indicate ways to overcome cellular unresponsiveness to the drug and thus lead to better treatment results. We used the budding yeast



*Saccharomyces cerevisiae* as a model organism to identify and characterize novel genes involved in cisplatin-induced cell kill, and found that SKY1 (SR-protein-specific kinase from budding yeast) is a cisplatin sensitivity gene whose disruption conferred cisplatin resistance. In cross-resistance studies, we observed resistance of yeast sky1DELTA cells (i.e., cells from which the SKY1 gene had been disrupted) to cisplatin, carboplatin (but not oxaliplatin), doxorubicin and daunorubicin, and hypersensitivity to cadmium chloride and 5-fluorouracil. Furthermore, these cells did not display reduced platinum accumulation, DNA platination or doxorubicin accumulation, indicating that the resistance is unrelated to decreased drug import or increased drug export. Based on the modification of the anticancer drug sensitivity profile and our finding that sky1DELTA cells display a mutator phenotype, we propose that Sky1p might play a significant role in specific repair and/or tolerance pathways. Disruption of the *S. cerevisiae* SKY1 gene would thus result in deregulation of such mechanisms and, consequently, lead to altered drug sensitivity.

CC Biochemistry studies - General 10060  
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062  
 Biochemistry studies - Minerals 10069  
 Pathology - Therapy 12512  
 Pharmacology - General 22002  
 Neoplasms - Pathology, clinical aspects and systemic effects 24004  
 Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts  
 Pharmacology; Tumor Biology

IT Chemicals & Biochemicals  
 5-fluorouracil; calcium chloride; carboplatin:  
 antineoplastic-drug; cisplatin: antineoplastic-drug; daunorubicin:  
 antineoplastic-drug; doxorubicin: antineoplastic-drug

IT Miscellaneous Descriptors  
 mutator phenotype

ORGN Classifier  
 Ascomycetes 15100  
 Super Taxa  
 Fungi; Plantae  
 Organism Name  
*Saccharomyces cerevisiae*  
 Taxa Notes  
 Fungi, Microorganisms, Nonvascular Plants, Plants

RN 51-21-8 (5-fluorouracil)  
 10043-52-4 (calcium chloride)  
 41575-94-4 (carboplatin)  
 15663-27-1 (cisplatin)  
 20830-81-3 (daunorubicin)  
 23214-92-8 (doxorubicin)

GEN *Saccharomyces cerevisiae* SKY1 gene (Ascomycetes)

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ACCESSION NUMBER: 2003464925 EMBASE Full-text  
 TITLE: Catheter occlusion by calcium carbonate during simultaneous infusion of 5-FU and calcium folinate.  
 AUTHOR: Bruch H.-R.; Esser M.  
 CORPORATE SOURCE: Dr. H.-R. Bruch, Praxis fur Hamatologie/Onkologie, Europaring 42, D-53123 Bonn, Germany. bonner-onkologen@online.de  
 SOURCE: Onkologie, (2003) Vol. 26, No. 5, pp. 469-472. .  
 Refs: 15  
 ISSN: 0378-584X CODEN: ONKOD2  
 COUNTRY: Germany

DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 016 Cancer  
 027 Biophysics, Bioengineering and Medical  
 Instrumentation  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English; German  
 ENTRY DATE: Entered STN: 1 Dec 2003  
 Last Updated on STN: 1 Dec 2003

AB Background: The treatment of colorectal cancer with administration of a 2-h infusion of calcium folinate followed by a 24-h infusion of 5-fluorouracil (5-FU) is a standard therapy. Based on newly published data we have applied an infusion of both compounds, 5-FU and calcium folinate, mixed together in an ambulatory pump. Patient and Methods: We report on a patient suffering from metastatic rectal cancer. After first and second line chemotherapy we started third line chemotherapy consisting of calcium folinate (1,000 mg) and 5-FU (4,000 mg) mixed together in a total volume of 240 ml in an ambulatory pump and administered over a period of 24 h. After a total of 11 applications the patient developed a port thrombosis resistant to lysis with urokinase. The blocked catheter was surgically explanted and the firm material inside was analyzed. Results: The material from inside the lumen of the catheter was analyzed using x-ray spectroscopy and a scanning electron microscopy. Both analyses confirmed that the isolated material is calcium carbonate. Conclusion: This case and the results of the analyses are in accordance with the described problems and results published earlier. A physical and/or chemical in vitro compatibility of 5-FU and calcium folinic acid, without validated clinical data is not sufficient to use this mixture in routine clinical practice.

CT Medical Descriptors:  
 \*vein occlusion: DT, drug therapy  
 \*vein occlusion: SI, side effect  
 \*thrombosis: DT, drug therapy  
 \*thrombosis: SI, side effect  
 \*rectum carcinoma: DT, drug therapy  
 \*liver metastasis: CO, complication  
 \*liver metastasis: DT, drug therapy  
 \*lung metastasis: CO, complication  
 \*lung metastasis: DT, drug therapy  
 catheter  
 drug infusion  
 infusion pump  
 cancer combination chemotherapy  
 dose response  
 drug effect  
 lysis  
 surgical technique  
 explant  
 histopathology  
 roentgen spectroscopy  
 scanning electron microscopy  
 anamnesis  
 disease course  
 phlebography  
 treatment outcome  
 human  
 male  
 case report  
 human tissue

adult

article

## Drug Descriptors:

\*calcium carbonate: EC, endogenous compound  
 \*fluorouracil: AE, adverse drug reaction  
 \*fluorouracil: CB, drug combination  
 \*fluorouracil: DO, drug dose  
 \*fluorouracil: DT, drug therapy  
 \*fluorouracil: PD, pharmacology  
 \*folinate calcium: AE, adverse drug reaction  
 \*folinate calcium: CB, drug combination  
 \*folinate calcium: DO, drug dose  
 \*folinate calcium: DT, drug therapy  
 \*folinate calcium: PD, pharmacology  
 urokinase: DT, drug therapy  
 urokinase: PD, pharmacology  
 antineoplastic agent: CB, drug combination  
 antineoplastic agent: DT, drug therapy  
 antineoplastic agent: PD, pharmacology  
 sodium derivative: CB, drug combination  
 sodium derivative: DT, drug therapy  
 sodium derivative: PD, pharmacology  
 sodium folinate: CB, drug combination  
 sodium folinate: DT, drug therapy  
 sodium folinate: PD, pharmacology  
     oxaliplatin: CB, drug combination  
     oxaliplatin: DT, drug therapy  
     oxaliplatin: PD, pharmacology  
     oxaliplatin: IV, intravenous drug administration  
 irinotecan: CB, drug combination  
 irinotecan: DT, drug therapy  
 irinotecan: PD, pharmacology  
 irinotecan: IV, intravenous drug administration  
 mitomycin: CB, drug combination  
 mitomycin: DT, drug therapy  
 mitomycin: PD, pharmacology  
 mitomycin: IV, intravenous drug administration  
 unclassified drug  
 sodiofolin  
 folinic acid

RN (calcium carbonate) 13397-26-7, 13701-58-1,  
 14791-73-2, 471-34-1; (fluorouracil) 51-21-8; (folinate calcium)  
 1492-18-8, 51057-63-7; (urokinase) 139639-24-0; (oxaliplatin)  
 61825-94-3; (irinotecan) 100286-90-6; (mitomycin) 1404-00-8; (folinic  
 acid) 58-05-9, 68538-85-2  
 CN (1) Sodiofolin; Leucovorin  
 NP (1) LV10  
 CO (1) Medac (Germany); (1) Baxter (Germany) ; Fresenius (Germany)

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ACCESSION NUMBER: 2003414953 EMBASE Full-text  
 TITLE: Oxaliplatin-safety profile: Neurotoxicity

AUTHOR: Grothey A.  
 CORPORATE SOURCE: Dr. A. Grothey, Division of Medical Oncology, Mayo Clinic,  
 200 First St, SW, Rochester, MN 55905, Germany  
 SOURCE: Seminars in Oncology, (2003) Vol. 30, No. 4 SUPPL. 15, pp.  
 5-13. .  
 Refs: 41

ISSN: 0093-7754 CODEN: SOLGAV  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Conference Article  
 FILE SEGMENT: 008 Neurology and Neurosurgery  
 016 Cancer  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 30 Oct 2003  
 Last Updated on STN: 30 Oct 2003

AB Oxaliplatin has become an integral part of various chemotherapy protocols, and in advanced colorectal cancer in particular. While oxaliplatin has only mild hematologic and gastrointestinal side effects, its dose-limiting toxicity is a cumulative sensory neurotoxicity that resembles that of cisplatin with the important difference of a more rapid and complete reversibility. The reversibility of neurotoxicity has been assured in long-term follow-up of patients who have received adjuvant oxaliplatin-based chemotherapy. In addition, oxaliplatin causes a very unique, but frequent, acute sensory neuropathy that is triggered or aggravated by exposure to cold but is rapidly reversible, without persistent impairment of sensory function. Various strategies have been proposed to prevent or treat oxaliplatin-induced neurotoxicity. The "Stop-and-Go" concept uses the reversibility of neurologic symptoms to aim at delivering higher cumulative oxaliplatin doses as long as the therapy is still effective. Several neuromodulatory agents such as calcium-magnesium infusions, antiepileptic drugs like carbamazepine or gabapentin, amifostine, alpha-lipoic acid, and glutathione have shown promising activity in prophylaxis and treatment of oxaliplatin-induced neurotoxicity. However, larger confirmatory trials are still lacking so that, to date, no evidence-based recommendation can be given for the prophylaxis of oxaliplatin-induced neurotoxicity. The predictability of neurotoxicity associated with oxaliplatin-based therapy should allow patients and doctors to develop strategies to manage this side effect in view of the individual patient's clinical situation. .COPYRGT. 2003 Elsevier Inc. All rights reserved.

CT Medical Descriptors:  
 \*drug safety  
 \*neurotoxicity: DT, drug therapy  
 \*neurotoxicity: ET, etiology  
 \*neurotoxicity: PC, prevention  
 \*neurotoxicity: SI, side effect  
 neuropathy: DT, drug therapy  
 neuropathy: ET, etiology  
 neuropathy: PC, prevention  
 neuropathy: SI, side effect  
 colorectal cancer: DT, drug therapy  
 blood toxicity: SI, side effect  
 maximum tolerated dose  
 gastrointestinal toxicity: SI, side effect  
 sensory dysfunction: DT, drug therapy  
 sensory dysfunction: ET, etiology  
 sensory dysfunction: PC, prevention  
 sensory dysfunction: SI, side effect  
 long term care  
 follow up  
 cancer chemotherapy  
 cancer adjuvant therapy  
 cold exposure  
 neuromodulation

chronic toxicity: SI, side effect  
 dose response  
 disease severity  
 pathogenesis  
 prophylaxis  
 drug infusion  
 neutropenia: SI, side effect  
 side effect: SI, side effect  
 nephrotoxicity: SI, side effect  
 nausea: SI, side effect  
 vomiting: SI, side effect  
 hypermagnesemia: SI, side effect  
 diarrhea: SI, side effect  
 drug fever: SI, side effect  
 drug hypersensitivity: SI, side effect  
 paresthesia: SI, side effect  
 dysesthesia: SI, side effect  
 muscle spasm: SI, side effect  
 ataxia: SI, side effect  
 urine retention: SI, side effect  
 ototoxicity: SI, side effect  
 human  
 clinical trial  
 conference paper  
 priority journal  
 Drug Descriptors:

\*oxaliplatin: AE, adverse drug reaction  
 \*oxaliplatin: CT, clinical trial  
 \*oxaliplatin: CB, drug combination  
 \*oxaliplatin: CM, drug comparison  
 \*oxaliplatin: DO, drug dose  
 \*oxaliplatin: DT, drug therapy  
 gluconate calcium: CT, clinical trial  
 gluconate calcium: CB, drug combination  
 gluconate calcium: DT, drug therapy  
 gluconate calcium: PD, pharmacology  
 magnesium chloride: CT, clinical trial  
 magnesium chloride: CB, drug combination  
 magnesium chloride: DT, drug therapy  
 anticonvulsive agent: AE, adverse drug reaction  
 anticonvulsive agent: CR, drug concentration  
 anticonvulsive agent: DT, drug therapy  
 anticonvulsive agent: PD, pharmacology  
 carbamazepine: AE, adverse drug reaction  
 carbamazepine: CR, drug concentration  
 carbamazepine: DT, drug therapy  
 carbamazepine: PD, pharmacology  
 gabapentin: DT, drug therapy  
 cisplatin: AE, adverse drug reaction  
 cisplatin: CM, drug comparison  
 fluorouracil: AE, adverse drug reaction  
 fluorouracil: CT, clinical trial  
 fluorouracil: CB, drug combination  
 fluorouracil: DT, drug therapy  
 folinic acid: AE, adverse drug reaction  
 folinic acid: CB, drug combination  
 folinic acid: DT, drug therapy  
 thioctic acid: DT, drug therapy  
 amifostine: CT, clinical trial  
 amifostine: DT, drug therapy

glutathione: CT, clinical trial  
 glutathione: CR, drug concentration  
 glutathione: DT, drug therapy  
 glutathione: IV, intravenous drug administration  
 RN (oxaliplatin) 61825-94-3; (gluconate calcium  
 ) 299-28-5; (magnesium chloride) 7786-30-3, 7791-18-6; (carbamazepine)  
 298-46-4, 8047-84-5; (gabapentin) 60142-96-3; (cisplatin) 15663-27-1,  
 26035-31-4, 96081-74-2; (fluorouracil) 51-21-8; (folinic acid) 58-05-9,  
 68538-85-2; (thioctic acid) 1077-29-8, 1200-22-2, 2319-84-8, 62-46-4;  
 (amifostine) 20537-88-6; (glutathione) 70-18-8  
 CN (1) Eloxatin  
 CO (1) Sanofi Synthelabo (United States)

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ACCESSION NUMBER: 1998269237 EMBASE Full-text  
 TITLE: Drug-induced urolithiasis.  
 AUTHOR: Hess B.  
 CORPORATE SOURCE: B. Hess, Department of Medicine, University Hospital,  
 CH-3010 Berne, Switzerland  
 SOURCE: Current Opinion in Urology, (1998) Vol. 8, No. 4, pp.  
 331-334. .  
 Refs: 23  
 ISSN: 0963-0643 CODEN: CUOUEQ  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; (Short Survey)  
 FILE SEGMENT: 028 Urology and Nephrology  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 27 Aug 1998  
 Last Updated on STN: 27 Aug 1998

AB Drugs can cause renal stone formation either by raising excretion rates of naturally occurring stone components or by directly precipitating within the urinary tract. In large series of analysed renal stones, the overall frequency of drug-induced urolithiasis is less than 0.5%. Five clinical presentations of drug-induced crystallization in the kidneys can be recognized: asymptomatic crystalluria, symptomatic crystalluria; stone passage; obstructive uropathy and tubulointerstitial nephritis. In the current literature review, the protease inhibitors used for treatment of patients infected with the human immunodeficiency virus stand out as a new class of drugs that frequently causes crystallization within the urinary tract. The most widely used compound, indinavir, may lead to crystalluria and renal stone formation in up to 50% of patients, and occasionally also causes acute renal failure caused by obstructive uropathy or tubulointerstitial nephritis. On the other hand, ritonavir appears more often to induce (reversible) acute renal failure than stone formation.

CT Medical Descriptors:  
 \*urolithiasis: ET, etiology  
 \*urolithiasis: SI, side effect  
 \*drug induced disease: ET, etiology  
 \*drug induced disease: SI, side effect  
 precipitation  
 crystalluria: SI, side effect  
 obstructive uropathy: SI, side effect  
 interstitial nephritis: SI, side effect  
 human immunodeficiency virus  
 acute kidney failure: DT, drug therapy

acute kidney failure: SI, side effect  
 calcium excretion  
 dysuria: SI, side effect  
 kidney colic: SI, side effect  
 nephrotoxicity: SI, side effect  
 fluid intake  
 drug urine level  
 liver  
 urine ph  
 hysterectomy  
 detrusor dyssynergia: CO, complication  
 detrusor dyssynergia: DT, drug therapy  
 urinary tract infection: CO, complication  
 urinary tract infection: DT, drug therapy  
 pseudomonas aeruginosa  
 hypercalcemia: SI, side effect  
 kidney calcification: SI, side effect  
 human  
 nonhuman  
     oral drug administration  
 intravenous drug administration  
 short survey  
 priority journal  
 Drug Descriptors:  
 proteinase inhibitor: AE, adverse drug reaction  
 proteinase inhibitor: DT, drug therapy  
 indinavir: AE, adverse drug reaction  
 indinavir: AD, drug administration  
 indinavir: CR, drug concentration  
 indinavir: DT, drug therapy  
 ritonavir: AE, adverse drug reaction  
 ritonavir: CB, drug combination  
 ritonavir: DT, drug therapy  
 ritonavir: TO, drug toxicity  
 saquinavir: AE, adverse drug reaction  
 saquinavir: CB, drug combination  
 saquinavir: DT, drug therapy  
 saquinavir: TO, drug toxicity  
 diltiazem: CB, drug combination  
 diltiazem: DT, drug therapy  
 foscarnet: CB, drug combination  
 foscarnet: TO, drug toxicity  
     calcium oxalate: EC, endogenous compound  
 glyoxylic acid: EC, endogenous compound  
 aminothiols: DT, drug therapy  
 penicillamine: AE, adverse drug reaction  
 penicillamine: DT, drug therapy  
 mercaptamine: DT, drug therapy  
 cysteine derivative: AD, drug administration  
 cysteine derivative: CB, drug combination  
 cysteine derivative: DT, drug therapy  
 citric acid: CB, drug combination  
 citric acid: DT, drug therapy  
 tosofloxacin: AE, adverse drug reaction  
 tosofloxacin: DT, drug therapy  
     calcium carbonate: AE, adverse drug reaction  
     calcium carbonate: DT, drug therapy  
 silicon dioxide  
 topiramate: AE, adverse drug reaction  
 topiramate: DT, drug therapy

carbonate dehydratase inhibitor: AE, adverse drug reaction

calcium phosphate: EC, endogenous compound

RN (proteinase inhibitor) 37205-61-1; (indinavir) 150378-17-9, 157810-81-6; (ritonavir) 155213-67-5; (saquinavir) 127779-20-8; (diltiazem) 33286-22-5, 42399-41-7; (foscarnet) 4428-95-9; (calcium oxalate) 563-72-4; (glyoxylic acid) 298-12-4; (penicillamine) 2219-30-9, 52-67-5; (mercaptamine) 156-57-0, 60-23-1; (citric acid) 126-44-3, 5949-29-1, 77-92-9, 8002-14-0; (tosufloxacin) 100490-36-6; (calcium carbonate) 13397-26-7, 13701-58-1, 14791-73-2, 471-34-1; (silicon dioxide) 10279-57-9, 14464-46-1, 14808-60-7, 15468-32-3, 60676-86-0, 7631-86-9; (topiramate) 97240-79-4; (calcium phosphate) 10103-46-5, 13767-12-9, 14358-97-5, 7758-87-4

L75 ANSWER 19 OF 21 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-09768 DRUGU T V Full-text

TITLE: Screening, prevention and socioeconomic costs associated with the treatment of colorectal cancer.

AUTHOR: Redaelli A; Cranor C W; Okano G J; Reese P R

CORPORATE SOURCE: Pharmacia

LOCATION: Milan, It.; Morrisville; Cary, N.C., USA

SOURCE: PharmacoEconomics (21, No. 17, 1213-38, 2003) 7 Tab. 132 Ref.  
ISSN: 1170-7690

AVAIL. OF DOC.: Pharmacia Corporation, Via R. Koch 1/2, Milan, 20152, Italy.  
(e-mail: alberto.redaelli@pharmacia.com).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The screening, prevention and socioeconomic costs associated with the treatment of colorectal cancer are reviewed. The management of colorectal cancer with respect to screening and surveillance procedures, diagnosis, prognosis, prevention (dietary and lifestyle issues and chemoprevention) and treatment, and economic burden of colorectal cancer (general treatment costs, screening, surveillance and diagnostic costs and chemotherapy-related costs) are described. Potential avenues to pursue in order to contain or reduce the economic burden of colorectal cancer would be the design and implementation of efficient screening programmes, improvement of patient awareness and compliance with screening guidelines, development of appropriate prevention program (primary and secondary), and earlier diagnosis.

L75 ANSWER 20 OF 21 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-44943 DRUGU T S Full-text

TITLE: Prevention of oxaliplatin peripheral sensory neuropathy by Ca+ gluconate/ Mg+ chloride infusions: a retrospective study.

AUTHOR: Gamelin E; Gamelin L; Delva R; Guerin Meyer V; Morel A; Boisdron Celle M

LOCATION: Angers, Fr.

SOURCE: ; Proc.Am.Soc.Clin.Oncol. (21, Pt. 1, 157a, 2002)  
CODEN: ; 7790

AVAIL. OF DOC.: CRLCC Paul Papin, Angers, France.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB Oxaliplatin (OXP) induces both acute and chronic neurotoxicity. Converging preclinical data suggest that acute symptoms are an acquired channelopathy.



Increased neuronal excitability may be due to action of OXP on voltage-dependent Na-channels and/or chelation of calcium by oxalate (OXP metabolite). In 101 advanced colorectal cancer patients treated with 5-fluorouracil (5FU)/OXP, infusions of Ca gluconate/Mg chloride before and after 5FU/OXP, reduced the incidence and intensity of acute neurosensory symptoms and may reduce cumulative neurotoxicity, allowing better dose-intensity and longer treatment duration. A prospective multicenter, randomized, double-blind, placebo-controlled study is underway to confirm the efficacy of Ca/Mg infusions. (conference abstract: 38th Annual Meeting of the American Society of Clinical Oncology, Orlando, Florida, USA, 2002).

L75 ANSWER 21 OF 21 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN

ACCESSION NUMBER: 1987-24175 DRUGU P V Full-text

TITLE: Calcium and Vitamin D Modulate Mouse Colon Epithelial Proliferation and Growth Characteristics of a Human Colon Tumor Cell Line.

AUTHOR: Wargovich M J; Lointier P H

LOCATION: Houston, Texas, United States

SOURCE: Can.J.Physiol.Pharmacol. (65, No. 3, 472-77, 1987) 3 Fig. 3  
Tab. 41 Ref.

CODEN: CJPPA3 ISSN: 0008-4212

AVAIL. OF DOC.: Section of Gastrointestinal Oncology and Digestive Diseases, Department of Medical Oncology, The University of Texas M.D. Anderson Hospital and Tumor Institute at Houston, Houston, TX, U.S.A. 77030.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The role of calcium and vitamin D (VD) in the prevention of colorectal cancer is reviewed. Animal studies have shown selected dietary lipids induce cellular proliferation in the colon and promote development of colon cancer. Colonic irritation induced by deoxycholic acid (DC) may be alleviated by calcium treatment and dietary calcium binders may interfere with the ability of calcium to regulate DNA synthesis, cell division and maintenance of membrane integrity. VD, apart from its role in calcium transport, may influence differentiation of cancer cells that have receptors for vitamin D3 or 1-alpha,25(OH)2D3. Calcium and VD are potential candidates for use in humans in clinical chemoprevention trials. (congress).

=> d his nofile

(FILE 'HOME' ENTERED AT 08:31:32 ON 04 AUG 2007)

FILE 'HCAPLUS' ENTERED AT 08:31:50 ON 04 AUG 2007

L1 1 SEA ABB=ON PLU=ON US20050148661/PN  
D ALL  
SEL RN

FILE 'REGISTRY' ENTERED AT 08:32:45 ON 04 AUG 2007

L2 11 SEA ABB=ON PLU=ON (10043-52-4/BI OR 11116-97-5/BI OR  
135701-98-3/BI OR 144-62-7/BI OR 299-28-5/BI OR 33659-28-8/BI  
OR 471-34-1/BI OR 61825-94-3/BI OR 7439-95-4/BI OR 7440-70-2/BI  
OR 7487-88-9/BI)  
L3 1 SEA ABB=ON PLU=ON 61825-94-3/RN  
L4 1 SEA ABB=ON PLU=ON OXALIPLATIN/CN  
L5 0 SEA ABB=ON PLU=ON OXALATE/CN  
E OXALATE/CN  
L6 1 SEA ABB=ON PLU=ON OXALIC ACID/CN  
D RN  
L7 1 SEA ABB=ON PLU=ON 144-62-7/RN  
L8 2 SEA ABB=ON PLU=ON L3 OR L4 OR L6 OR L7  
L9 9 SEA ABB=ON PLU=ON L2 NOT L8

FILE 'ZCAPLUS' ENTERED AT 08:38:06 ON 04 AUG 2007

L10 QUE ABB=ON PLU=ON OXALATE OR OXALIC ACID  
L11 QUE ABB=ON PLU=ON OXALIPLATIN  
L12 QUE ABB=ON PLU=ON CALCIUM (2A) (GLUCONATE OR CHLORIDE OR  
BROMOGALACTOGLUCONATE OR CARBONATE)  
L13 QUE ABB=ON PLU=ON MAGNESIUM (2A) (SULFATE OR PIDOLATE)  
L14 QUE ABB=ON PLU=ON CANCER? OR NEOPLAS? OR TUMOR? OR TUMOUR?  
L15 QUE ABB=ON PLU=ON ANTIVIRAL? OR ANTI(W)VIRAL? OR VIRUS? OR  
ANTIVIRUS? OR ANTI(W)VIRUS?  
L16 QUE ABB=ON PLU=ON ?VIRUS? OR ?VIRAL?  
L17 QUE ABB=ON PLU=ON NEUROTOXIC?  
L18 QUE ABB=ON PLU=ON GAMELIN L?/AU  
L19 QUE ABB=ON PLU=ON GAMELIN E?/AU  
L20 QUE ABB=ON PLU=ON BOISDRON CELLE M?/AU  
L21 QUE ABB=ON PLU=ON MOREL A?/AU  
L22 QUE ABB=ON PLU=ON AY<2004 OR PY<2004 OR PRY<2004 OR MY<2004  
OR REVIEW/DT  
L23 QUE ABB=ON PLU=ON AY<2004 OR PY<2004 OR PRY<2004

FILE 'HCAPLUS' ENTERED AT 08:43:10 ON 04 AUG 2007

FILE 'STNGUIDE' ENTERED AT 08:43:32 ON 04 AUG 2007

FILE 'HCAPLUS' ENTERED AT 08:46:29 ON 04 AUG 2007

L24 56622 SEA ABB=ON PLU=ON L10 OR L11  
L25 62777 SEA ABB=ON PLU=ON L8 OR L24  
L26 623520 SEA ABB=ON PLU=ON L9  
L27 110313 SEA ABB=ON PLU=ON CALCIUM/OBI (2A) (GLUCONATE/OBI OR  
CHLORIDE/OBI OR BROMOGALACTOGLUCONATE/OBI OR CARBONATE/OBI)  
L28 19480 SEA ABB=ON PLU=ON MAGNESIUM/OBI (2A) (SULFATE/OBI OR  
PIDOLATE/OBI)  
L29 635324 SEA ABB=ON PLU=ON L27 OR L28 OR L26  
L30 4522 SEA ABB=ON PLU=ON L25 AND L29  
L31 59 SEA ABB=ON PLU=ON L30 AND L14

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L32 37 SEA ABB=ON PLU=ON L30 AND (L15 OR L16)  
 L33 8 SEA ABB=ON PLU=ON L30 AND L17

FILE 'HCAPLUS' ENTERED AT 08:54:35 ON 04 AUG 2007

L34 82 SEA ABB=ON PLU=ON L31 OR L32 OR L33  
 L35 1 SEA ABB=ON PLU=ON L34 AND L1  
 L36 67 SEA ABB=ON PLU=ON L34 AND L22  
 L37 1444895 SEA ABB=ON PLU=ON 1/SC, SX  
 L38 38 SEA ABB=ON PLU=ON L36 AND L37

FILE 'HCAPLUS' ENTERED AT 08:58:53 ON 04 AUG 2007

L39 1286494 SEA ABB=ON PLU=ON (TREAT#/OBI OR TREATMENT#/OBI OR PREVENT?/OBI OR CURE#/OBI)  
 L40 20 SEA ABB=ON PLU=ON L38 AND L39

FILE 'HCAPLUS' ENTERED AT 09:02:52 ON 04 AUG 2007

L41 254740 SEA ABB=ON PLU=ON INJECT?/OBI OR ORAL?/OBI  
 L42 13 SEA ABB=ON PLU=ON L38 AND L41

FILE 'HCAPLUS' ENTERED AT 09:05:21 ON 04 AUG 2007

SAVE TEMP L42 KUD318HCAP/A

L43 9 SEA ABB=ON PLU=ON GAMELIN L?/AU  
 L44 53 SEA ABB=ON PLU=ON GAMELIN E?/AU  
 L45 32 SEA ABB=ON PLU=ON BOISDRON CELLE M?/AU  
 L46 499 SEA ABB=ON PLU=ON MOREL A?/AU  
 L47 551 SEA ABB=ON PLU=ON L43 OR (L44 OR L45 OR L46)  
 L48 53 SEA ABB=ON PLU=ON L44 AND (L45 OR L46 OR L47)  
 L49 32 SEA ABB=ON PLU=ON L45 AND (L46 OR L47)  
 L50 4 SEA ABB=ON PLU=ON L43 AND L44 AND L45 AND L46  
 L51 23 SEA ABB=ON PLU=ON L47 AND L48 AND L49  
 L52 23 SEA ABB=ON PLU=ON L50 OR L51  
 L53 1 SEA ABB=ON PLU=ON L52 AND L1  
 L54 22 SEA ABB=ON PLU=ON L52 NOT L1  
 L55 13 SEA ABB=ON PLU=ON L54 AND L22

SAVE TEMP L55 KUD318HCAPIN/A

FILE 'STNGUIDE' ENTERED AT 09:09:51 ON 04 AUG 2007

FILE 'MEDLINE, BIOSIS, EMBASE, BIOTECHNO, DRUGU' ENTERED AT 09:14:57 ON 04 AUG 2007

L56 52321 SEA ABB=ON PLU=ON L24  
 L57 61889 SEA ABB=ON PLU=ON L27  
 L58 18226 SEA ABB=ON PLU=ON L28  
 L59 78565 SEA ABB=ON PLU=ON L57 OR L58  
 L60 947 SEA ABB=ON PLU=ON L56 AND L59  
 L61 53 SEA ABB=ON PLU=ON L60 AND L14  
 L62 5 SEA ABB=ON PLU=ON L60 AND L15  
 L63 10 SEA ABB=ON PLU=ON L60 AND L16  
 L64 25 SEA ABB=ON PLU=ON L60 AND L17  
 L65 63 SEA ABB=ON PLU=ON (L61 OR L62 OR L63 OR L64)  
 L66 42 SEA ABB=ON PLU=ON L39 AND L65  
 L67 25 SEA ABB=ON PLU=ON L41 AND L65  
 L68 47 SEA ABB=ON PLU=ON L66 OR L67  
 L69 17 SEA ABB=ON PLU=ON L68 NOT L13  
 L70 9 SEA ABB=ON PLU=ON L69 AND L22  
 SAVE TEMP L70 KUD318MULTI/A  
 L71 15 SEA ABB=ON PLU=ON L50  
 L72 14 SEA ABB=ON PLU=ON L50 NOT L70  
 L73 3 SEA ABB=ON PLU=ON L72 AND L22

10/501318

SAVE TEMP L72 KUD318MULTIN/A

FILE 'STNGUIDE' ENTERED AT 09:23:28 ON 04 AUG 2007

D QUE L55

D QUE L72

FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 09:24:54 ON 04  
AUG 2007

L74           19 DUP REM L55 L72 (8 DUPLICATES REMOVED)  
              ANSWERS '1-13' FROM FILE HCAPLUS  
              ANSWERS '14-15' FROM FILE MEDLINE  
              ANSWERS '16-17' FROM FILE BIOSIS  
              ANSWER '18' FROM FILE EMBASE  
              ANSWER '19' FROM FILE DRUGU  
              D 1-13 IBIB AB  
              D 14-19 IBIB AB  
              D QUE L42  
              D QUE L70  
L75           21 DUP REM L42 L70 (1 DUPLICATE REMOVED)  
              ANSWERS '1-13' FROM FILE HCAPLUS  
              ANSWER '14' FROM FILE MEDLINE  
              ANSWER '15' FROM FILE BIOSIS  
              ANSWERS '16-18' FROM FILE EMBASE  
              ANSWERS '19-21' FROM FILE DRUGU  
              D 1-13 IBIB ED AB HITIND  
              D 14-21 IBIB AB HITIND